

Supplementary information

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Supplementary Table S1 Average concentration of serological indices during five periods

Serological Indices	1	2	3	4	5
E(pg/mL)	53.41±9.55 ^{ab}	35.54±7.34 ^a	53.79±6.01 ^b	47.32±15.27 ^{ab}	33.86±18.35 ^{ab}
FSH(mIU/ml)	6.22±0.78	5.58±2.03	5.65±0.76	5.11±1.16	6.06±1.85
T4(ng/mL)	171.3±45.91	195.72±32.07	191.0±22.52	228.85±13.68	169.58±38.95
CT(pg/mL)	45.37±4.49	50.40±1.51	41.55±7.98	36.99±12.48	41.99±10.24
GH(ng/mL)	15.18±2.76 ^{ab}	15.48±4.10 ^{ab}	12.77±2.79 ^a	18.34±1.80 ^b	16.98±3.66 ^{ab}
PROG(pmol/L)	1004.89±84.05	1151.87±361.95	1102.88±378.04	1155.23±199.43	1107.32±306.62
TSH(mU/L)	9.97±2.11 ^{ab}	11.12±2.94 ^{ab}	11.85±2.34 ^{ab}	9.33±1.13 ^a	13.16±1.46 ^b

Note: Values in the same row with the same or no letter superscripts mean no significant difference ($p > 0.05$), while with different small letter superscripts mean significant different ($p < 0.05$).

Supplementary Table S2 Summary statistics for sequence quality of 30 samples

Samples	Raw Reads (10 ⁶)	Raw bases (10 ⁶)	Clean Reads (10 ⁶)	Clean bases (10 ⁶)	Q20 (%)	Q30 (%)	GC content (%)
1-1-o	48.71	7355.73	45.58	6883.05	97.22	92.84	51.99
1-1-h	44.88	6776.65	42.11	6359.27	97.06	92.39	49.78
1-2-o	45.95	6937.83	42.88	6475.32	97.22	92.75	50.72
1-2-h	44.93	6784.03	42.10	6357.15	96.91	92.09	49.86
1-3-o	48.27	7288.34	45.18	6822.24	97.01	92.36	51.33
1-3-h	43.15	6515.45	40.38	6097.26	97.12	92.58	49.83
2-1-o	46.43	7011.22	43.35	6545.67	97.17	92.59	50.31
2-1-h	49.69	7503.31	46.57	7031.88	97.13	92.6	50.01
2-2-o	42.92	6480.30	40.16	6063.80	96.95	92.15	50.38
2-2-h	47.44	7164.17	44.44	6711.19	97.12	92.56	49.99
2-3-o	43.25	6531.05	40.43	6104.54	97.18	92.61	50.44
2-3-h	48.43	7312.23	45.61	6886.87	97.14	92.62	49.93
3-1-o	40.87	6130.03	37.91	5686.19	97.68	94.24	50.54
3-1-h	41.72	6258.21	38.75	5812.03	97.55	93.96	49.25
3-2-o	42.48	6372.62	39.22	5882.57	97.16	92.55	49.39
3-2-h	44.55	6682.44	41.36	6203.45	97.62	94.01	49.33
3-3-o	38.63	5794.97	35.95	5392.27	97.69	94.21	49.53
3-3-h	41.55	6232.85	38.54	5781.74	97.41	93.59	49.48
4-1-o	43.33	6498.75	40.40	6060.07	96.97	92.73	50.21
4-1-h	50.82	7622.77	47.42	7113.36	96.67	92.11	49.64
4-2-o	46.53	6979.16	43.48	6522.42	96.91	92.51	49.81
4-2-h	53.53	8029.17	49.99	7498.31	96.81	92.39	49.76
4-3-o	46.65	6997.53	43.60	6539.85	97.03	92.67	49.46
4-3-h	51.22	7682.71	48.03	7204.12	96.77	92.25	49.48
5-1-o	53.25	7987.22	49.03	7353.82	97.72	93.96	47.86

5-1-h	47.07	7060.75	43.73	6558.82	97.65	93.84	47.48
5-2-o	49.82	7472.76	46.11	6916.56	97.72	93.94	47.58
5-2-h	44.44	6666.10	41.34	6200.93	97.41	93.38	47.39
5-3-o	50.34	7551.63	46.18	6926.70	97.35	93.3	48.14
5-3-h	45.91	6886.34	42.70	6404.44	97.51	93.58	47.28

Note: i-j-o (i=1,2,3,4,5; j=1,2,3) represent ovary samples from 3 biological replicas in 5 periods;

i-j-h (i=1,2,3,4,5; j=1,2,3) represent hypothalamus samples from 3 biological replicas in 5 periods.

Supplementary Table S3 DEGs between 10 groups in the hypothalamus and ovary

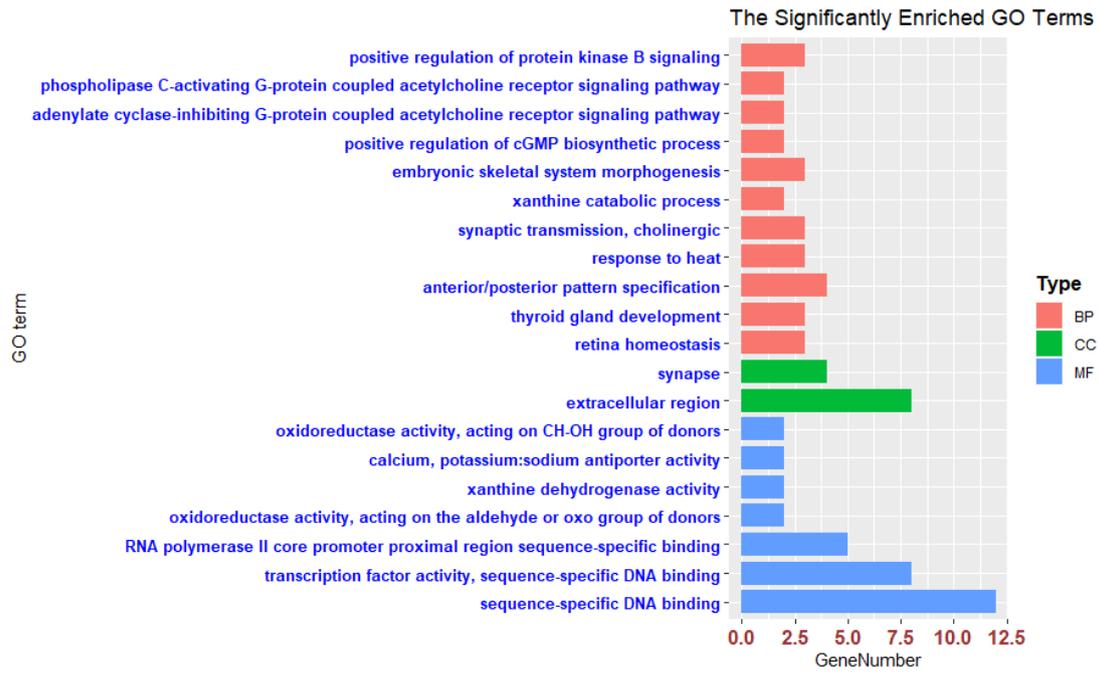
Period	Tissue	Down-regulated genes	Up-regulated genes	Total DEGs
1-vs-2	hypothalamus	71	113	184
	ovary	173	200	373
1-vs-3	hypothalamus	310	1179	1489
	ovary	842	1688	2530
1-vs-4	hypothalamus	197	344	541
	ovary	380	808	1188
1-vs-5	hypothalamus	68	118	186
	ovary	577	431	1008
2-vs-3	hypothalamus	158	932	1090
	ovary	326	875	1201
2-vs-4	hypothalamus	99	226	325
	ovary	35	143	178
2-vs-5	hypothalamus	13	10	23
	ovary	40	26	66
3-vs-4	hypothalamus	486	100	586
	ovary	420	153	573
3-vs-5	hypothalamus	941	124	1065
	ovary	721	161	882
4-vs-5	hypothalamus	217	74	291
	ovary	152	41	193

Supplementary Table S4 DEGs whose expression trends were consistent with ELR were related to aging, autophagy or apoptosis, development

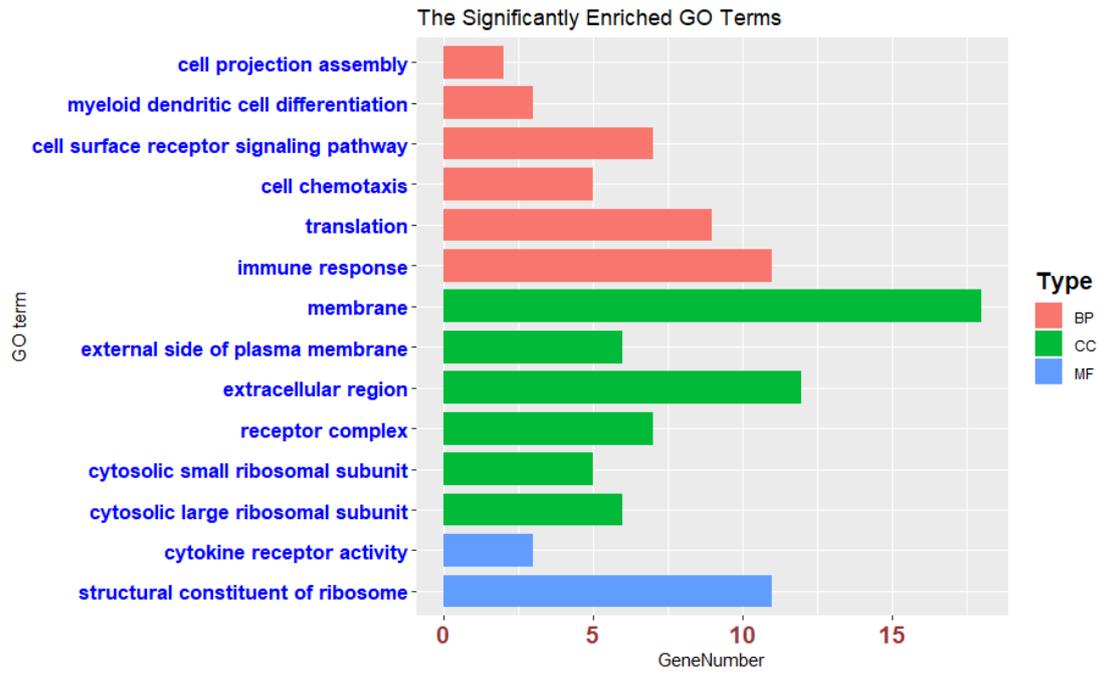
Genes function (Numbers)	Genes and corresponding references
cell aging (45)	<i>ABCB8</i> [1], <i>BMP8A</i> [2], <i>BOLA3</i> [3], <i>CCK</i> [4], <i>CDKN1C</i> [5, 6], <i>CFD</i> [7], <i>COX5A</i> [8], <i>FAM171A2</i> [9], <i>FBXO46</i> [10], <i>FGFR4</i> [11, 12], <i>FMC1</i> [13], <i>FOXC1</i> [14], <i>FOXL2</i> [15, 16], <i>FZD5</i> [17], <i>GGCX</i> [18], <i>HIF3A</i> [19], <i>HNRNPA0</i> [20], <i>IGFBP4</i> [21], <i>MANF</i> [22], <i>MRPS12</i> [23], <i>MTERF4</i> [24], <i>NAT8B</i> [25], <i>NEDD8</i> [26], <i>NOG</i> [27], <i>NOG2</i> [28], <i>PABPNI</i> [29], <i>POLD4</i> [30], <i>POLE4</i> [31], <i>PPP1R1B</i> [32], <i>RAD9A</i> [33], <i>RBM8A</i> [34], <i>RPL35A</i> [35], <i>SELENOH</i> [36], <i>SEMA6C</i> [37], <i>SNCB</i> [38], <i>SOCSI</i> [39, 40], <i>SREBF1</i> [41], <i>SST</i> [42], <i>SUV39HI</i> [43], <i>TAPI</i> [44], <i>TCN2</i> [45], <i>TINAGLI</i> [46], <i>UCP3</i> [47, 48], <i>ZARI</i> [49], <i>ZC3H10</i> [50]
cell autophagy or apoptosis (8)	<i>ANKRD39</i> [34], <i>CBLN4</i> [34], <i>GRN</i> [51], <i>PAXX</i> [52], <i>PPIL1</i> [53], <i>S100A16</i> [54], <i>SCYLI</i> [55], <i>TGFBI</i> [56]
Cell development (12)	<i>ACP5</i> [57], <i>ADAMTS4</i> [58, 59], <i>CARTPT</i> [60, 61], <i>CDK5R1</i> [62], <i>CDK5R2</i> [63], <i>FJXI</i> [64], <i>GTPBP3</i> [65], <i>H2AFV</i> [66], <i>HSD17B1</i> [67], <i>RENBP</i> [68], <i>VSTM2L</i> [69], <i>WBP1</i> [70]

Supplementary Table S5 Top five genes in the network of the top 100 brown genes ranked by the MCC method

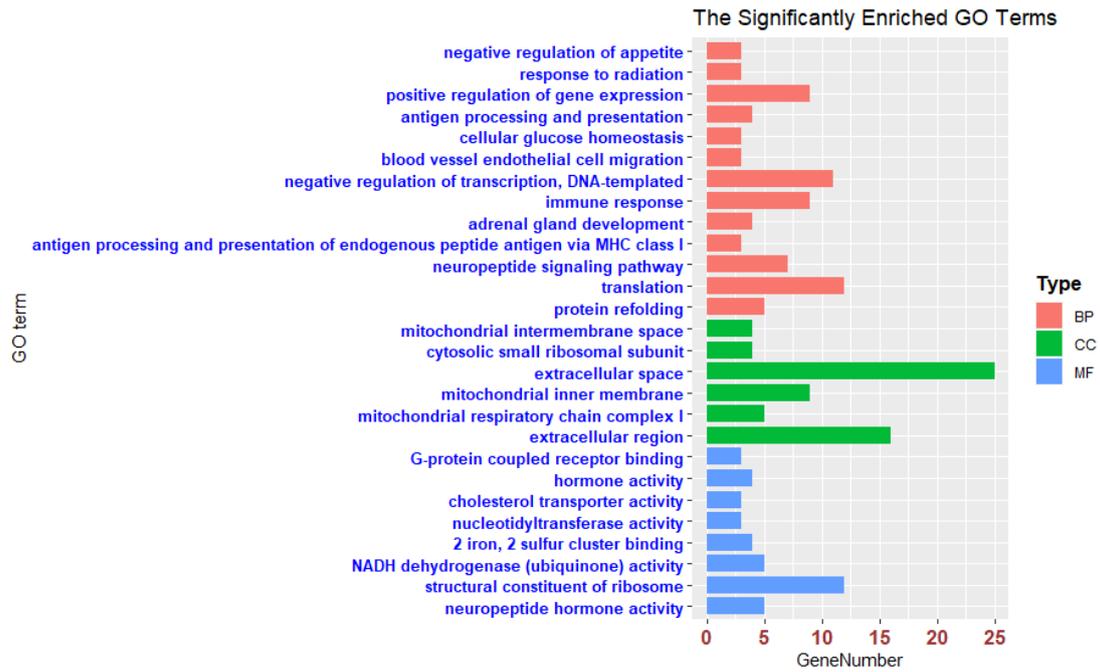
Rank	Name	Score	Description
1	<i>INO80D</i>	38	INO80 complex subunit D
2	<i>HELZ</i>	10	helicase with zinc finger
3	<i>AGO4</i>	2	argonaute RISC component 4
3	<i>ROCK2</i>	2	Rho associated coiled-coil containing protein kinase 2
3	<i>RFX7</i>	2	regulatory factor X7



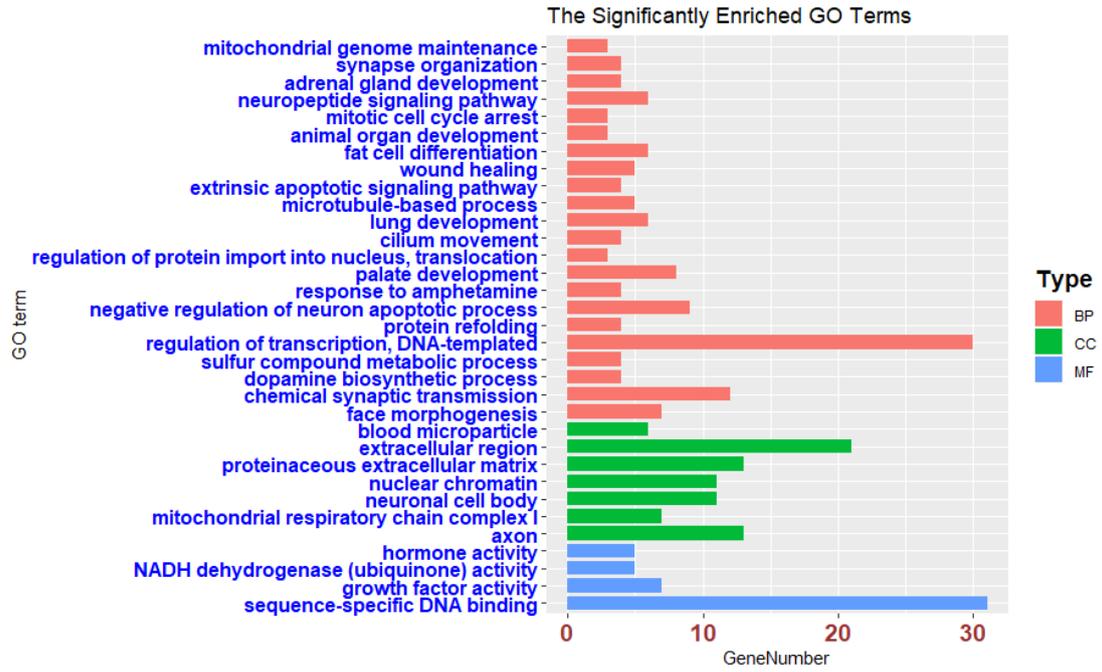
Supplementary Figure S1 Significant GO enrichment of DEGs ($P < 0.05$) for comparison of 1-vs-2 in the hypothalamus.



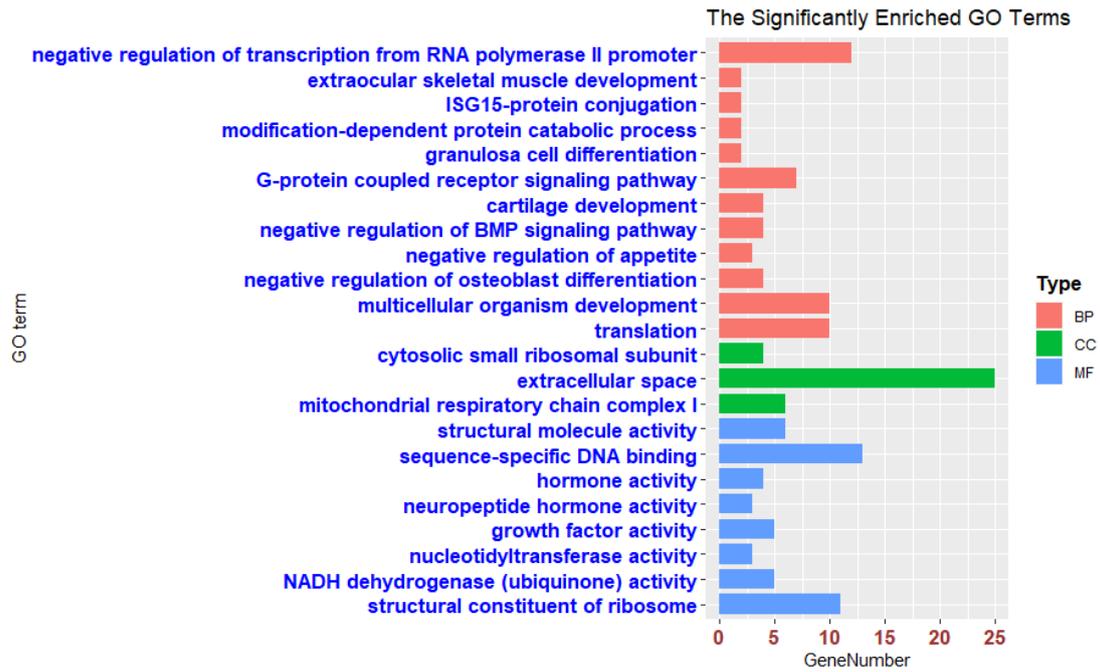
Supplementary Figure S2 Significant GO enrichment of DEGs ($P < 0.05$) for comparison of 1-vs-2 in the ovary.



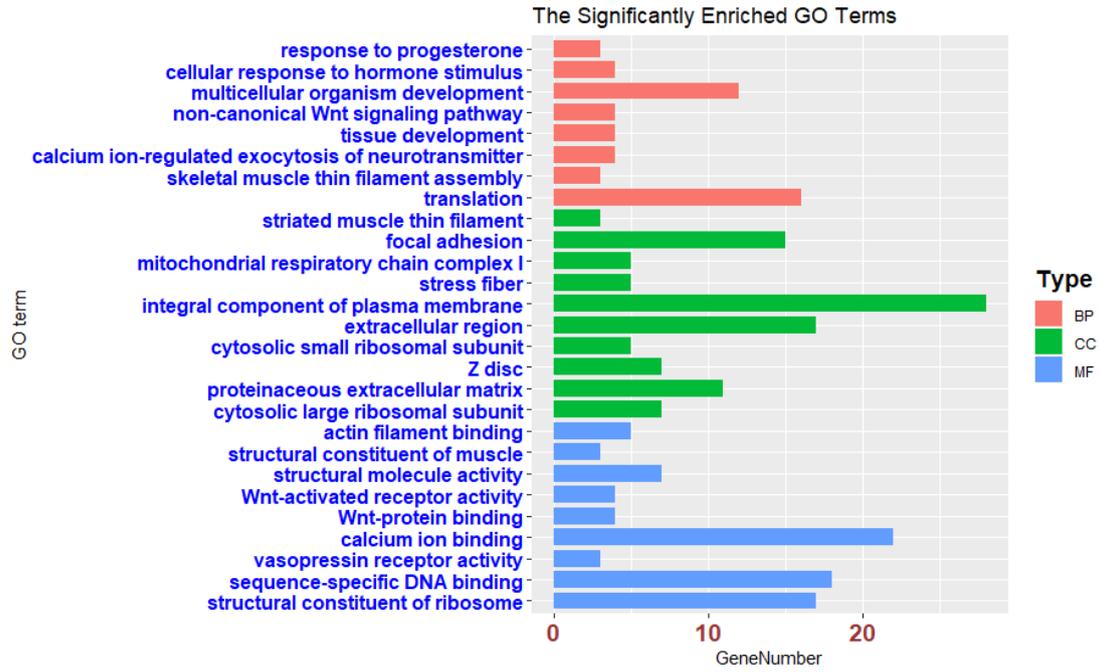
Supplementary Figure S3 Significant GO enrichment of DEGs ($P < 0.05$) for comparison of 2-vs-3 in the hypothalamus.



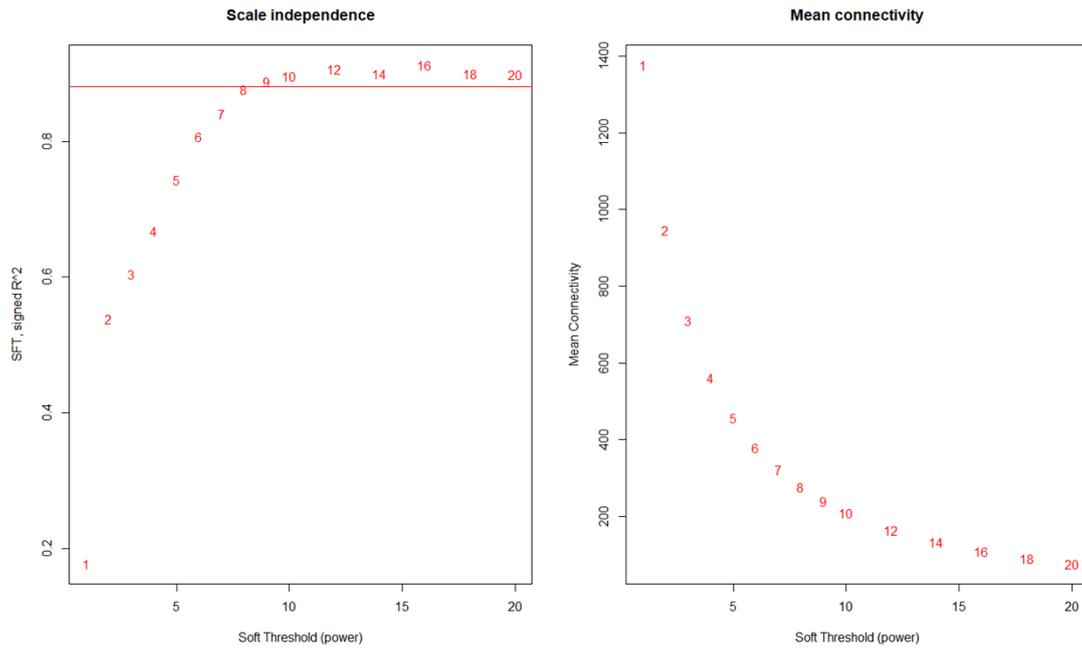
Supplementary Figure S4 Significant GO enrichment of DEGs ($P < 0.05$) for comparison of 2-vs-3 in the ovary.



Supplementary Figure S5 Significant GO enrichment of DEGs ($P < 0.05$) for comparison of 3-vs-5 in the hypothalamus.



Supplementary Figure S6 Significant GO enrichment of DEGs ($P < 0.05$) for comparison of 3-vs-5 in the ovary.



Supplementary Figure S7 Determination of the soft threshold ($\beta=8$). The left panel shows the analysis of scale-free fit index and the right panel refers to the analysis of mean connectivity.

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