

Supplementary Information

Regulation of gene expression by the APP family in the adult cerebral cortex

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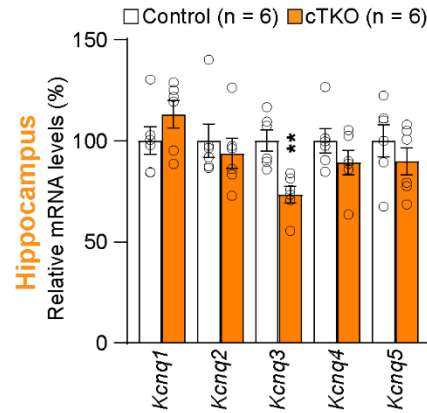
- 1) Supplementary Table S1
- 2) Supplementary Table S2
- 3) Supplementary Figure S1
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	RIN	Number of input reads	Number of uniquely mapped reads	Percentage of uniquely mapped reads
Neocortex				
Control 1	9.6	34886565	31744914	90.99%
Control 2	9.8	24389920	21925932	89.90%
Control 3	8.1	17582967	15857094	90.18%
Control 4	8.6	22801453	20413272	89.53%
Control 5	9.1	21320896	19162851	89.88%
cTKO 1	8.5	31272184	28441499	90.95%
cTKO 2	8.7	29265688	26340178	90.00%
cTKO 3	8.5	23139692	20616224	89.09%
cTKO 4	9.0	27636580	24831316	89.85%
cTKO 5	8.9	19242730	17120400	88.97%
Hippocampus				
Control 1	9.4	27674630	24394426	88.15%
Control 2	9.6	33684563	29293392	86.96%
Control 3	8.7	33162854	28511942	85.98%
Control 4	9.6	30798851	26951482	87.51%
Control 5	9.2	28749829	25192799	87.63%
cTKO 1	8.7	35140528	30473193	86.72%
cTKO 2	8.3	31842882	28053570	88.10%
cTKO 3	9.2	37185953	32378392	87.07%
cTKO 4	9.8	28335592	25006294	88.25%
cTKO 5	9.0	34329516	30141227	87.80%

Supplementary Table S1. RNA integrity number (RIN) of RNA samples and mapping rate of reads generated by RNA-seq of the neocortex and hippocampus of controls and cTKO mice at the age of 3 months

Gene name	logFC	Neocortex		logFC	Hippocampus	
		p-value	FDR p-value		p-value	FDR p-value
<i>App</i>	-2.099	7.91E-113	1.10E-108	-1.778	1.26E-80	1.73E-76
<i>Aplp1</i>	-1.921	2.18E-70	1.51E-66	-1.931	1.62E-71	1.11E-67
<i>Aplp2</i>	-1.604	1.76E-54	8.11E-51	-1.247	3.92E-26	7.67E-23
<i>Rskr</i>	-0.836	1.85E-08	1.60E-05	-1.184	1.21E-04	1.14E-02
<i>Npas4</i>	-0.807	5.57E-10	8.56E-07	-1.380	2.13E-08	8.33E-06
<i>Vwa3a</i>	-0.802	2.14E-08	1.74E-05	-1.749	2.79E-13	2.74E-10
<i>Btg2</i>	-0.695	9.35E-08	5.63E-05	-0.484	4.60E-04	2.98E-02
<i>Map3k19</i>	-0.605	7.46E-05	1.13E-02	-0.632	3.36E-04	2.40E-02
<i>Hmgcs2</i>	-0.568	1.23E-04	1.51E-02	-0.714	8.18E-05	8.83E-03
<i>Hrk</i>	-0.520	3.36E-06	1.11E-03	-0.731	5.72E-07	1.51E-04
<i>Nrros</i>	-0.508	2.54E-04	2.59E-02	-0.604	1.81E-04	1.49E-02
<i>Homer2</i>	-0.507	1.85E-05	4.06E-03	-0.585	1.45E-04	1.29E-02
<i>Rims1</i>	-0.493	1.01E-09	1.40E-06	-0.362	7.40E-04	4.04E-02
<i>Ppfia3</i>	-0.478	4.40E-09	4.68E-06	-0.334	4.63E-04	2.98E-02
<i>Cdkl4</i>	-0.451	3.95E-05	7.02E-03	-0.607	1.86E-05	2.66E-03
<i>Hlf</i>	-0.367	4.79E-04	3.95E-02	-0.596	5.42E-04	3.32E-02
<i>Prkcb</i>	-0.332	6.38E-06	1.84E-03	-0.396	7.39E-04	4.04E-02
<i>Tub</i>	-0.292	4.33E-04	3.66E-02	-0.417	4.51E-04	2.98E-02
<i>Ecm1</i>	0.517	3.62E-05	6.68E-03	0.648	5.25E-04	3.28E-02
<i>Npy</i>	0.569	1.11E-04	1.41E-02	1.263	4.22E-07	1.18E-04
<i>Serinc2</i>	0.586	8.25E-05	1.18E-02	1.275	6.98E-09	3.41E-06
<i>Ubt1</i>	0.630	5.67E-05	9.45E-03	0.581	1.81E-04	1.49E-02
<i>Serpinf1</i>	0.713	5.59E-08	3.69E-05	0.813	8.46E-05	8.99E-03
<i>Blnk</i>	0.718	6.15E-05	9.78E-03	0.824	4.02E-04	2.76E-02
<i>Plekha2</i>	0.724	1.96E-05	4.17E-03	0.840	7.62E-07	1.90E-04
<i>Rab32</i>	0.736	5.16E-04	4.18E-02	0.614	7.85E-04	4.19E-02
<i>Bdnf</i>	0.759	1.44E-05	3.49E-03	1.213	2.48E-08	9.42E-06
<i>Adamts18</i>	0.863	3.44E-04	3.27E-02	1.673	3.96E-16	4.94E-13
<i>Bmp3</i>	0.908	2.42E-08	1.76E-05	1.739	1.99E-11	1.51E-08
<i>Ccnf</i>	0.908	4.28E-04	3.66E-02	1.046	1.64E-05	2.48E-03
<i>Rxfp3</i>	0.945	1.41E-05	3.47E-03	1.064	1.03E-07	3.54E-05
<i>Tll1</i>	1.101	1.06E-07	6.10E-05	0.793	7.60E-04	4.13E-02
<i>Gldn</i>	1.117	2.03E-04	2.14E-02	1.993	3.37E-06	7.00E-04
<i>Als2</i>	1.125	1.04E-40	3.61E-37	2.196	1.62E-35	7.41E-32
<i>Gpnmb</i>	1.161	1.16E-06	4.48E-04	1.727	4.05E-12	3.47E-09
<i>Igsf9</i>	1.199	2.78E-09	3.49E-06	1.007	6.31E-05	7.15E-03
<i>Cxcr4</i>	1.201	5.00E-06	1.54E-03	0.901	8.89E-05	9.37E-03
<i>Col27a1</i>	1.261	7.91E-06	2.18E-03	1.042	5.00E-04	3.14E-02
<i>Prss23</i>	1.306	4.22E-07	1.82E-04	1.072	1.51E-05	2.38E-03
<i>Fndc9</i>	1.372	5.20E-06	1.56E-03	2.342	1.30E-04	1.18E-02
<i>Foxm1</i>	1.505	9.10E-05	1.22E-02	1.299	9.96E-05	1.01E-02
<i>Ecel1</i>	1.532	6.52E-11	1.50E-07	2.161	2.11E-13	2.23E-10
<i>Ly6g6e</i>	2.495	2.29E-08	1.76E-05	1.704	1.56E-07	5.10E-05
<i>Top2a</i>	2.650	6.53E-04	4.81E-02	2.612	1.57E-04	1.37E-02
<i>H19</i>	5.824	6.12E-07	2.57E-04	5.108	8.42E-05	8.99E-03

Supplementary Table S2. List of common DEGs between the neocortex and hippocampus



Supplementary Figure S1. Reduced mRNA levels of *Kcnq3* in the hippocampus of cTKO mice

Quantification of the relative expression of the Kv7 channel encoding genes in the hippocampus of cTKO mice and controls at the age of 3 months. Among Kv7 channel encoding genes, only the *Kcnq3* mRNA levels were significantly decreased in cTKO mice compared with controls (26.61%, $p = 0.0024$, Student's *t*-test, $n = 6$ per genotype). The mRNA levels of each gene were normalized to the *Gapdh* and *Rpl13a* housekeeping mRNA levels. All data expressed as means $\pm$ SEMs. Statistical analysis was performed with Student's *t*-test. ** $p < 0.01$.

Primer ID	Sequence (5'-3')	Target Gene
JKM1698	TTGTCTCCTGCGACTTCA	<i>Gapdh</i> -Forward
JKM1699	TCCACCACCCTGTTGCTGTA	<i>Gapdh</i> -Reverse
JKM1700	AGGGGCAGGTTCTGGTATTG	<i>Rpl13a</i> -Forward
JKM1701	TGTTGATGCCTTCACAGCGT	<i>Rpl13a</i> -Reverse
APP-101	GCCATCATCGGACTCATGGT	<i>APP</i> -Forward
APP-201	ATCCGTTCTGCTGCATCTTG	<i>APP</i> -Reverse
APLP1-101	CTGAGAAGGCCCAGCAGAT	<i>APLP1</i> -Forward
APLP1-201	ACCCAAGTGTTTCAGCAAGGA	<i>APLP1</i> -Reverse
APLP2-101	AGGAACAGCTGGAAATTCGA	<i>APLP2</i> -Forward
APLP2-201	GCTGGATGAGGGTCTGTCTT	<i>APLP2</i> -Reverse
JKM1482	TGGACATCATTCGCAACTACAC	<i>Kai1</i> -Forward-#1
JKM1483	GCATGGGTAAGTGGTCTTGGA	<i>Kai1</i> -Reverse-#1
JKM1484	CTTCAGGAGAACTTCGGCATC	<i>Kai1</i> -Forward-#2
JKM1485	AGAATGAATGTACCGGCACAAA	<i>Kai1</i> -Reverse-#2
JKM1486	TGGCAGCAAGGTAACCACAG	<i>Gsk3b</i> -Forward-#1
JKM1487	CGGTTCTTAAATCGCTTGTCCTG	<i>Gsk3b</i> -Reverse-#1
JKM1488	AAGCGATTTAAGAACCGAGAGC	<i>Gsk3b</i> -Forward-#2
JKM1489	AGAAATACCGCAGTCGGAATAT	<i>Gsk3b</i> -Reverse-#2
JKM1492	GGAACCCATCTCGGCATCC	<i>Bace1</i> -Forward-#1
JKM1493	TCCGATTCCTCGTCGGTCTC	<i>Bace1</i> -Reverse-#1
JKM1494	CAGTGGGACCACCAACCTTC	<i>Bace1</i> -Forward-#2
JKM1495	GCTGCCTTGATGGACTTGAC	<i>Bace1</i> -Reverse-#2
JKM1498	TCCCGGTCCAGATCACACTC	<i>Tip60</i> -Forward-#1
JKM1499	ACCTTCCGTTTCGTTGAGCG	<i>Tip60</i> -Reverse-#1
JKM1500	AGAGAGGTGAAACGGAAGGTG	<i>Tip60</i> -Forward-#2
JKM1501	TGGTGCTGACGGTATTCCATC	<i>Tip60</i> -Reverse-#2
JKM1576	TCTTGTAAGCAGCCTCAGCC	<i>Nep</i> -Forward-#1
JKM1577	ACATAAAGCCTCCCCACAGC	<i>Nep</i> -Reverse-#1
JKM1578	ATTCAGCCAAAGCAAGCAGC	<i>Nep</i> -Forward-#2
JKM1579	TGAAGAATGGGGGCTGCAAA	<i>Nep</i> -Reverse-#2
JKM1510	CCGGGGAGTTGTCTTTCGTG	<i>P53</i> -Forward-#1
JKM1511	AATGTGAGGGAAGAGAGTTCCA	<i>P53</i> -Reverse-#1
JKM1512	GTCACAGCACATGACGGAGG	<i>P53</i> -Forward-#2
JKM1513	TCTTCCAGATGCTCGGGATAC	<i>P53</i> -Reverse-#2
JKM1516	GCCATCTGGGCCAAAGATAACC	<i>Egfr</i> -Forward-#1
JKM1517	GTCTTCGCATGAATAGGCCAAT	<i>Egfr</i> -Reverse-#1
JKM1518	GCATCATGGGAGAGAACAACA	<i>Egfr</i> -Forward-#2
JKM1519	TCAGGAACCATTAATCCATAGGT	<i>Egfr</i> -Reverse-#2
JKM1522	ACTATGGATGCCCTAAACTTG	<i>Lrp1</i> -Forward-#1
JKM1523	GCAATCTCTTTCACCGTCACA	<i>Lrp1</i> -Reverse-#1

JKM1524	CAGAGATGCCCGCCAAATGA	<i>Lrp1</i> -Forward-#2
JKM1525	CGTCAAAATCTTTGCACGTCTTG	<i>Lrp1</i> -Reverse-#2
JKM1528	AGCCAGTCGGCCATTAACG	<i>Fe65</i> -Forward-#1
JKM1529	GCACACTACCCTCTCCCATAG	<i>Fe65</i> -Reverse-#1
JKM1530	AGGAGGCCCAATGGAGTT	<i>Fe65</i> -Forward-#2
JKM1531	GCGCACAGCGAAACACTTG	<i>Fe65</i> -Reverse-#2
JKM1534	GCTGGAAAATCCCTCGGACA	<i>vGlut2</i> -Forward-#1
JKM1535	GCATAGCGGAGCCTTCTTCT	<i>vGlut2</i> -Reverse-#1
JKM1536	GTCTTTGGGGCTGCGATACT	<i>vGlut2</i> -Forward-#2
JKM1537	CATGACAGGCTGGGTAGGTG	<i>vGlut2</i> -Reverse-#2
JKM1584	CTGCTCAACACCCAGGACAT	<i>X11</i> -Forward-#1
JKM1585	GTTGGCAGAATGGATCCCCA	<i>X11</i> -Reverse-#1
JKM1586	CAGAGAAGTCGGGGAAGCTG	<i>X11</i> -Forward-#2
JKM1587	GGTCCGGCCTCCTTATTAGC	<i>X11</i> -Reverse-#2
JKM1596	GCACCTCTTCCTTCCCTGAC	<i>Npas4</i> -Forward-#1
JKM1597	GATTGGGGCTCAGTTGCTCT	<i>Npas4</i> -Reverse-#1
JKM1600	ACCCTGTACCTTGCAACAA	<i>Npas4</i> -Forward-#2
JKM1601	GCAAACCCTTCGTAGGGGAA	<i>Npas4</i> -Reverse-#2
JKM1604	TGAGGACACAGAGGCAGGTA	<i>Rskr</i> -Forward
JKM1605	GCTGGTCCAGTTCAAAAGCG	<i>Rskr</i> -Reverse
JKM999	CACTGACAGAGATCCGCAGAA	<i>Vwa3a</i> -Forward
JKM1000	GCAAGCCAGTCTTCAGAGTCT	<i>Vwa3a</i> -Reverse
JKM1255	ATGAGCCACGGGAAGAGAAC	<i>Btg2</i> -Forward
JKM1256	GCCCTACTGAAAACCTTGAGTC	<i>Btg2</i> -Reverse
JKM1211	GGTGGCCTTGGATACTTCTGA	<i>Map3k19</i> -Forward
JKM1212	GCACGTCCCTAGATAAGCTACTA	<i>Map3k19</i> -Reverse
JKM1203	GAAGAGAGCGATGCAGGAAAC	<i>Hmgcs2</i> -Forward
JKM1204	GTCCACATATTGGGCTGGAAA	<i>Hmgcs2</i> -Reverse
JKM1608	CGACGAGCTGCACCGA	<i>Hrk</i> -Forward
JKM1609	CTACGCGCTCCGCCT	<i>Hrk</i> -Reverse
JKM1235	ATTCTGGATGCTAACCCCTCTCA	<i>Nrros</i> -Forward
JKM1236	GCGTAGTGGCTGATACGGT	<i>Nrros</i> -Reverse
JKM1239	CGTTTTGACAGTTTGATACAGCC	<i>Homer2</i> -Forward
JKM1240	CAGACACACTCTTTTACGCAGA	<i>Homer2</i> -Reverse
JKM561	CAAACCCTAGCCACCCAG	<i>Rims1</i> -Forward
JKM562	CAGGTGTAGATTGGAGCCAG	<i>Rims1</i> -Reverse
JKM1277	GGCCAACTCAAGATGGTGGA	<i>Ppfia3</i> -Forward
JKM1278	GGTCTGGCTTTCTTCCCTCC	<i>Ppfia3</i> -Reverse
JKM1231	CTGCTGGACAGTGCCTACTT	<i>Cdkl4</i> -Forward
JKM1232	CATCAGGTGTGGGGGAGATG	<i>Cdkl4</i> -Reverse
JKM983	CCGGCTTCAGCACTATGAAC	<i>Hlf</i> -Forward

JKM984	ACGAATGACAATCCTTGTGTCTC	<i>Hlf</i> -Reverse
JKM1259	TGGCAAGGTCATGCTCTCAG	<i>Prkcb</i> -Forward
JKM1260	TCACAAAGTACAGGCGGTCC	<i>Prkcb</i> -Reverse
JKM1263	GGAGCCCCTAGGAAGGAGAA	<i>Tub</i> -Forward
JKM1264	AGTCAAGATCTGCACTGGGC	<i>Tub</i> -Reverse
JKM1345	TGCCACTACCCTCCTAGTCC	<i>Ecm1</i> -Forward
JKM1346	CATGAGGTTGGGGGTGACTC	<i>Ecm1</i> -Reverse
JKM194	CTCCGCTCTGCGACACTAC	<i>Npy</i> -Forward
JKM195	GGAAGGGTCTTCAAGCCTTGT	<i>Npy</i> -Reverse
JKM897	TGCCCCTCCTGGAATCAG	<i>Serinc2</i> -Forward
JKM898	ACTCCGTGTAGTAGACGAACAT	<i>Serinc2</i> -Reverse
JKM1323	GAGCCCTTGAAGAAGGAGCG	<i>Ubtd1</i> -Forward
JKM1324	AGCTCGTCATAGCATTACAAA	<i>Ubtd1</i> -Reverse
JKM1335	GCCCTGGTGCTACTCCTCT	<i>Serpinf1</i> -Forward
JKM1336	CGGATCTCAGGCGGTACAG	<i>Serpinf1</i> -Reverse
JKM903	GCCCTCCAAGTGTTCCTCG	<i>Blnk</i> -Forward
JKM904	GGCAGGCATCACATACATCTC	<i>Blnk</i> -Reverse
JKM359	TCTGAAGGACTGGGTAGAAGC	<i>Plekha2</i> -Forward
JKM360	CTGATAGGCGTTTGTACCACC	<i>Plekha2</i> -Reverse
JKM1610	GCGTGGGTAAGACGAGCATC	<i>Rab32</i> -Forward
JKM1611	GTTGAGAACTTTGAGGGCGAA	<i>Rab32</i> -Reverse
JKM537	TCATACTTCGGTTGCATGAAGG	<i>Bdnf</i> -Forward
JKM538	AGACCTCTCGAACCTGCCC	<i>Bdnf</i> -Reverse
JKM1614	TATTTACACGACATTTTGCACC	<i>Adamts18-1</i> -Forward
JKM1615	ACGAGTTCCATTAGAGCAGGG	<i>Adamts18-1</i> -Reverse
JKM877	AGCACACGAGCTACCCAAG	<i>Bmp3</i> -Forward
JKM878	GTAAGCTGGATACCACGCTTTC	<i>Bmp3</i> -Reverse
JKM1375	GAAGGACTTTACAAGCCTGTGT	<i>Ccnf</i> -Forward
JKM1376	CCAGGGCGGAAATGATCTCC	<i>Ccnf</i> -Reverse
JKM1618	TCCTCATCAGCGCGGTTTAC	<i>Rxfp3</i> -Forward
JKM1619	CAGTGCCAGGTTAGTGACAAAG	<i>Rxfp3</i> -Reverse
JKM1622	GGTTGGTGGTCTCGGGTATTG	<i>Tll1</i> -Forward
JKM1623	GGCGATGTCACCCCAAAACA	<i>Tll1</i> -Reverse
JKM1626	ACCAGGCCACAATGGATCAG	<i>Gldn</i> -Forward
JKM1627	GGTAGACCCAGTTCACCAGC	<i>Gldn</i> -Reverse
JKM032	CCTGGTTATGGGAGGATTCCA	<i>Als2</i> -Forward
JKM033	CACACGAAACCTACCACTTCAAA	<i>Als2</i> -Reverse
JKM1379	AGCCAATAGGAAACTGCCCC	<i>Gpnmb</i> -Forward
JKM1380	TCCTTCTCCTGGTCTCCTCG	<i>Gpnmb</i> -Reverse
JKM1295	GGCTGCGCTTTGGATTCT	<i>Igsf9</i> -Forward
JKM1296	GACAACTCTTACCCACGTAATCG	<i>Igsf9</i> -Reverse

JKM1630	GAAGTGGGGTCTGGAGACTAT	<i>Cxcr4</i> -Forward
JKM1631	TTGCCGACTATGCCAGTCAAG	<i>Cxcr4</i> -Reverse
JKM1339	CCTTGGCATCCCATCCAGTT	<i>Col27a1</i> -Forward
JKM1340	AAGATCTCCCCTCCCTGGTC	<i>Col27a1</i> -Reverse
JKM919	GGTGAGTCCCTACACCGTTC	<i>Prss23</i> -Forward
JKM920	GGCGTCGAAGTCTGCCTTAG	<i>Prss23</i> -Reverse
JKM1355	AGGAGCCATCATCTCCTGGT	<i>Fndc9</i> -Forward
JKM1356	GAAGGAGCGAGGTGTTCCAA	<i>Fndc9</i> -Reverse
JKM1636	GCCTGTCTCCTCCACTCCTA	<i>Foxm1</i> -Forward
JKM1637	GGTTTCGTACTGGGCTGAAA	<i>Foxm1</i> -Reverse
JKM1385	TCTACAACCAGCGCGTGAAT	<i>Ecel1</i> -Forward
JKM1386	CACCAGTTCTGTGCAAAGGC	<i>Ecel1</i> -Reverse
JKM879	TACTGGTCACGGTCCTACTCT	<i>Ly6g6e</i> -Forward
JKM880	GGCAGCATTGCATAGGTCCT	<i>Ly6g6e</i> -Reverse
JKM1640	GAGTGCTCGTGTCTCGGAAA	<i>Top2a</i> -Forward
JKM1641	TTTGCTTTCTTGCTCGTGGC	<i>Top2a</i> -Reverse
JKM1644	CTGCTCCAAGGTGAAGCTGA	<i>H19</i> -Forward
JKM1645	TAGAGGCTTGGCTCCAGGAT	<i>H19</i> -Reverse
JKM1714	ACCTCATCGTGGTTGTAGCCT	<i>Kcnq1</i> -Forward
JKM1715	GGATACCCCTGATAGCTGATGT	<i>Kcnq1</i> -Reverse
JKM1460	TACCAGCTTTGGAGGTCTCTT	<i>Kcnq2</i> -Forward
JKM1461	ACAGTGTGGAAACACAGCAGA	<i>Kcnq2</i> -Reverse
JKM1720	CATCCCAGCAGTCTCCAAGG	<i>Kcnq3</i> -Forward
JKM1721	TGCATGTCCACGAGGAAGTC	<i>Kcnq3</i> -Reverse
JKM1718	TTGAGCAGTATTCAGCAGGACA	<i>Kcnq4</i> -Forward
JKM1719	GGACCCTTATCGCCCTTCTC	<i>Kcnq4</i> -Reverse
JKM1470	AAGACTGAGGTTTGCTCGAAAA	<i>Kcnq5</i> -Forward
JKM1471	TGTAGGAACCGGAGACTTCTG	<i>Kcnq5</i> -Reverse

Supplementary Table S3. List of primer used in this study