

Overlapping functions of Rbbp4 and Rbbp7 in regulating cell proliferation and histone H3.3 deposition during mouse preimplantation development

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Figure Legends

Figure S1 Functional redundancy for Rbbp4 and 7 in supporting mouse preimplantation development.

A. Representative pictures of NC and R4KD, R7KD, and coKD embryos at E3.5 and E4.5. B and C. Outgrowth analysis showed significant reduction in percent outgrowth in KD groups (three replicates). Asterisks refer to significant differences ($P < 0.05$).

Figure S2 RNA-seq analysis. A-D. Scatter plots showing correlation of two biological replicates of RNA-seq samples for NC, R4KD, R7KD, and coKD embryos at morula stage. E. Gene ontology analysis of up-regulated genes induced in coKD embryos compared with NC embryos.

Figure S3 Effects of individual knockdown of Rbbp4 or 7 in cell cycle progression and intercellular junctions in preimplantation embryos. A. Immunostaining against Phosphorylation of S10 on histone H3 (pH3S10), an established marker for G2/M phase, in NC, R4KD, and R7KD blastocyst. B. Immunostaining analysis of Phosphorylation of Rb (pRb), a marker for G1/S checkpoint, in NC, R4KD, and R7KD blastocyst. C. The number of intercellular junctions is reduced obviously in coKD relative to NC embryos. Scale bar = 50 μ M.

Figure S4 Effects of individual knockdown of Rbbp4 or 7 in cell apoptosis and genome stability in preimplantation embryos.

A. Cell apoptosis analysis of NC, R4KD, and R7KD blastocyst. B. Representative pictures of immunostaining against Histone H2AX phosphorylation (rH2AX), a marker for DNA damage, in NC, R4KD, and R7KD blastocyst.

Figure S5 Effects of individual knockdown of Rbbp4 or 7 in lineage development in preimplantation embryos.

A. Immunostaining analysis of Oct4, a marker of trophectoderm, and Gata6, a marker for primitive endoderm, in NC, R4KD, and R7KD blastocyst at E4.25. B. Immunostaining analysis of Sox17, a marker for primitive endoderm, in NC, R4KD, and R7KD blastocyst at E4.25.

Figure S6 Effects of Rbbp4/7 depletion on histone H3 lysine 27 acetylation and (H3K27ac) and histone H4 lysine 16 acetylation (H4K16ac). A. Immunostaining analysis of H4K16ac in NC and coKD morula. B. Immunostaining analysis of H3K27ac in NC and coKD morula. C. Immunostaining analysis of H3K27ac in NC, R4KD, and R7KD blastocysts. Scale bar = 50 μ M

Figure S7 Effects of Rbbp4/7 depletion on histone H3 lysine 4 tri-methylation (H3K4me3) and histone H3 lysine 9 di-methylation (H3K9me2). A and B. Immunostaining analysis of H3K4me3 (A) and H3K9me2 (B), hallmarks for active and repressive transcription, respectively. Scale bar = 50 μ M.

Figure S8 Effects of Rbbp4/7 depletion on histone variant H3.3. A and B. Immunostaining analysis of H.3 in NC, R4KD, and R7KD morula (A) and blastocysts (B). Scale bar = 50 μ M

Figure S9 Reproducibility of H3K27ac ChIP-seq experiment. A and B. Scatter plots showing correlation of two biological replicates of H3K27ac ChIP-seq samples for NC and coKD embryos at morula stage.

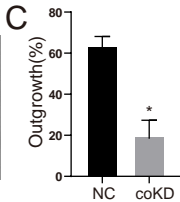
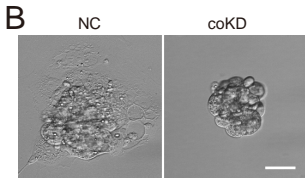
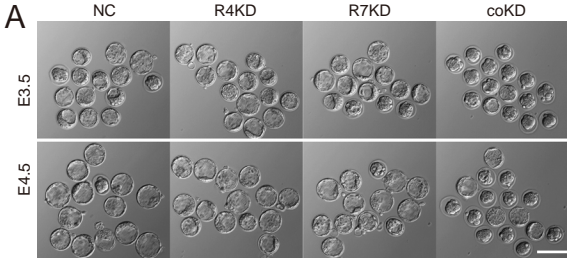
Table S1: siRNA information

Table S2: Antibody information

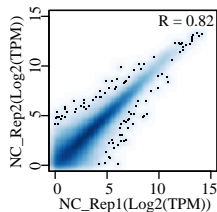
Table S3. Differentially expressed genes identified by RNA-seq between Rbbp4 depleted group and control group in mice (ranked by adjusted p (padj) value). Threshold: $\text{padj} \leq 0.05$ & $\text{FoldChange} \geq 1.5$ or $\text{FoldChange} \leq -1.5$.

Table S4. Differentially expressed genes identified by RNA-seq between Rbbp7 depleted group and control group in mice (ranked by adjusted p (padj) value). Threshold: $\text{padj} \leq 0.05$ & $\text{FoldChange} \geq 1.5$ or $\text{FoldChange} \leq -1.5$.

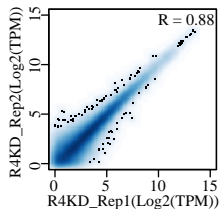
Table S5. Differentially expressed genes identified by RNA-seq between both RBBP4 and 7 depleted group and control group in mice (ranked by adjusted p (padj) value). Threshold: $\text{padj} \leq 0.05$ & $\text{FoldChange} \geq 1.5$ or $\text{FoldChange} \leq -1.5$.



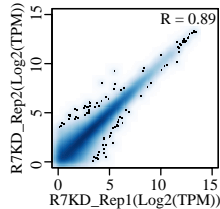
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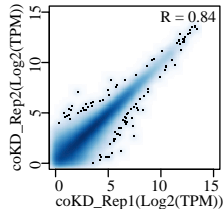
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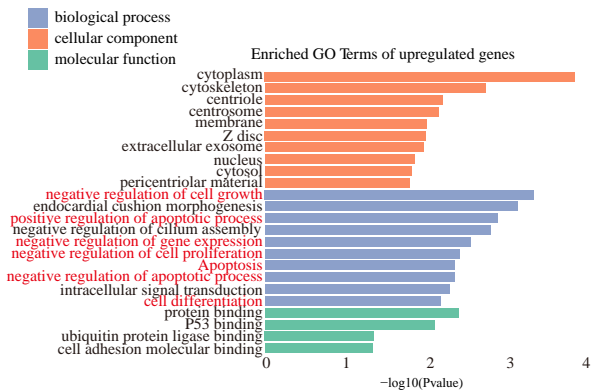
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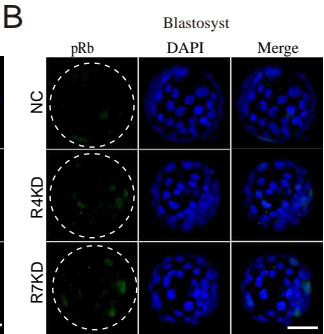
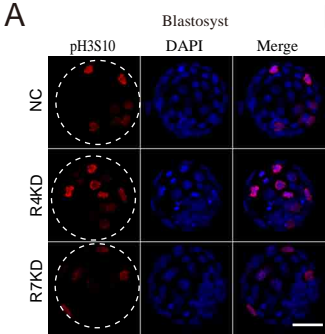


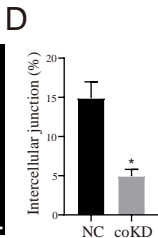
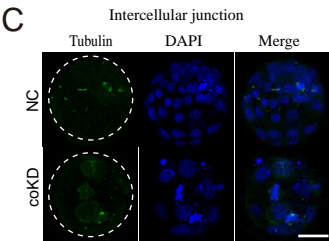
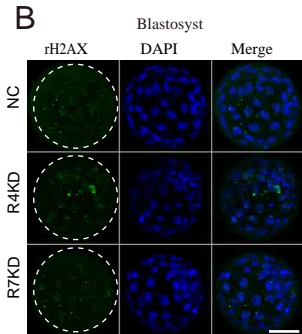
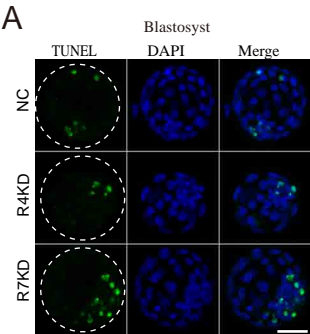
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E







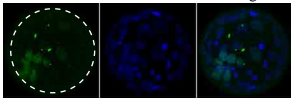
A

Oct4

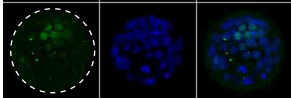
DAPI

Merge

NC



R4KD



R7KD

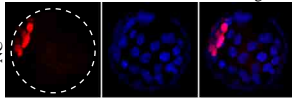
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Sox17

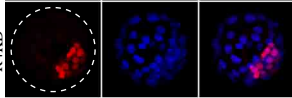
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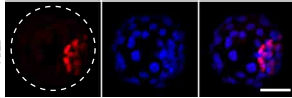
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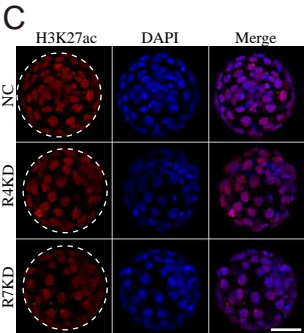
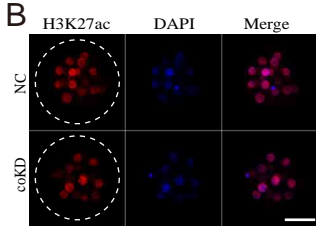
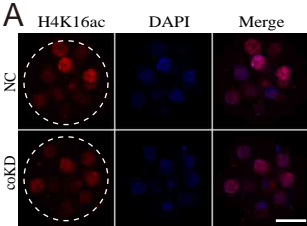


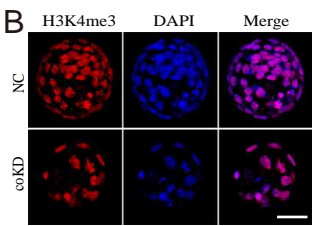
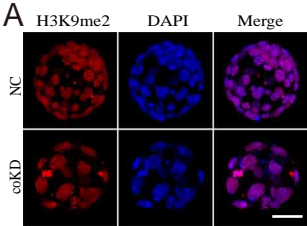
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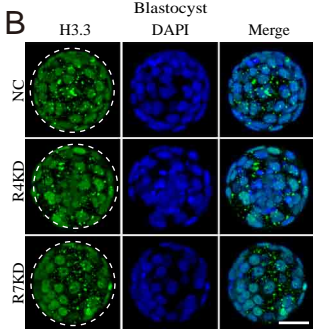
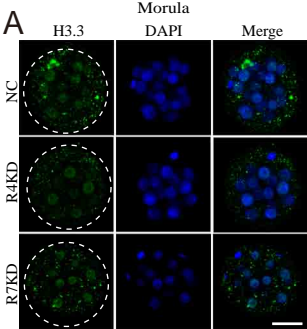


R7KD









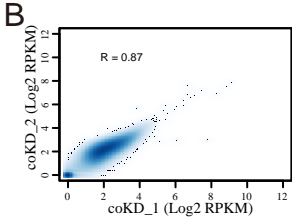
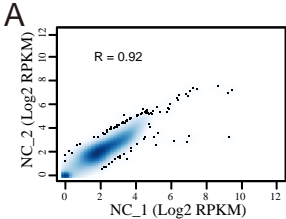


Table S1 : siRNA information

Name	Species	Sequences (5' to 3')
Rbbp4-Mus-526	Mouse	Sense: CCCGGUACAUGCCUCAGAATT Antisense: UUCUGAGGCAUGUACCGGGTT
Rbbp4-Mus-609	Mouse	Sense: CCUUCUAAACCAGACCCUUTT Antisense: AAGGGUCUGGUUUAGAAGGTT
Rbbp4-Mus-901	Mouse	Sense: GGGACACUCGUUCAACAATT Antisense: UUGUUUGAACGAGUGUCCCTT
Rbbp7-Mus-419	Mouse	Sense: GGUUAUGACCCAUGCUCUUTT Antisense: AAGAGCAUGGGUCAUAAACCTT
Rbbp7-Mus-888	Mouse	Sense: GGGCAUCUCCUGAGUGCAUTT Antisense: AUGCACUCAGGAGAUGCCCTT
Rbbp7-Mus-1028	Mouse	Sense: GCUGCAUGAGUCCUUGUUUTT Antisense: AAACAAGGACUCAUGCAGCTT

Table S2 : Antibody information

Name	Host	Company	Catalog Number	Application
RBBP4	Rabbit	Abcam	ab79416	IF (1:200)
RBBP7	Rabbit	Cell Signaling Technology	#6882	IF (1:200)
Phospho-Histone H3 (Ser10)	Rabbit	Cell Signaling Technology	#3377	IF (1:200)
Phospho-Rb	Rabbit	Cell Signaling Technology	#85165	IF (1:200)
α -Tubulin	Rabbit	Cell Signaling Technology	#2125	IF (1:200)
OCT4	Mouse	Santa Cruz	sc-5279	IF (1:200)
SOX17	Goat	Bio-technie	AF1924	IF (1:200)
YAP	Mouse	Santa Cruz	sc-101200	IF (1:200)
γ -H2AX	Mouse	Abcam	ab26350	IF (1:200)
H3.3	Mouse	Abnova	H00003021-M01	IF (1:100)
H3K27ac	Rabbit	Active Motif	39133	IF (1:200)
H3k14ac	Rabbit	Abcam	ab52946	IF (1:200)
H4K16ac	Rabbit	Abcam	ab109463	IF (1:200)
H3K4me3	Rabbit	Cell Signaling Technology	#9751	IF (1:200)
H3K9me2	Rabbit	Cell Signaling Technology	#9753	IF (1:200)
H3K27me3	Mouse	Abcam	ab6002	IF (1:200)
TET1	Rat	Active Motif	6174161742	IF (1:200)
DNMT3B	Mouse	Novus Biologicals	52A1018	IF (1:200)
TEAD4	Mouse	Abcam	ab58310	IF (1:200)
HDAC1	Mouse	Cell Signaling Technology	#5356	IF (1:200)
HDAC2	Mouse	Cell Signaling Technology	#5113	IF (1:200)
Sin3a	Rabbit	Abcam	Ab129087	IF (1:200)
P53-acetyl-lys379	Rabbit	GeneTex	GTX88013	IF (1:200)
β -Catenin	Rabbit	Cell Signaling Technology	#8480	IF (1:200)
E-Cadherin	Rat	Sigma-Aldrich	U3254	IF (1:1000)
Donkey anti-Rabbit 594		Invitrogen	A21207	IF (1:100)
Goat anti-Mouse 488		Invitrogen	A11001	IF (1:100)
Donkey anti-Goat 594		Invitrogen	A11058	IF (1:100)
Goat anti-Rabbit 488		Invitrogen	A11008	IF (1:100)
Donkey anti- Rabbit 488		Invitrogen	A21206	IF (1:100)

Table S3. Differentially expressed genes identified by RNA-seq between Rbbp4 depleted group and control group in mice (ranked by adjusted p (padj) value). Threshold: padj<=0.05 & FoldChange>=1.5 or FoldChange <= -1.5.

	Gene.names	FoldChange	padj		Gene.names	FoldChange	padj
1	<i>Ndufa9</i>	-29.178168	0.000000	14	<i>Pank3</i>	-2.440767	0.000000
2	<i>Gm21293</i>	-10.445230	0.012721	15	<i>Max</i>	-2.290331	0.000015
3	<i>Rbbp4</i>	-9.696435	0.000000	16	<i>Cdkn1a</i>	-2.253246	0.000479
4	<i>Slc39a2</i>	-5.679754	0.012721	17	<i>Mob1a</i>	-2.169439	0.000069
5	<i>Sac3d1</i>	-3.020487	0.012721	18	<i>Dcbld2</i>	2.398497	0.000268
6	<i>Pafah1b2</i>	-2.716613	0.000000	19	<i>Acad10</i>	2.861932	0.048356
7	<i>Mfn2</i>	-2.701567	0.000268	20	<i>Plau</i>	2.946342	0.000000
8	<i>Plet1</i>	-2.654351	0.006280	21	<i>Cobll1</i>	3.081197	0.039153
9	<i>Znrd1</i>	-2.644248	0.049006	22	<i>Pcnt</i>	4.359551	0.000946
10	<i>Pigs</i>	-2.581545	0.012773	23	<i>Krt19</i>	5.660180	0.024327
11	<i>Vnn1</i>	-2.477782	0.008351	24	<i>Csnk2a3</i>	9.735482	0.003627
12	<i>Zfp367</i>	-2.451932	0.010616	25	<i>Arhgap33</i>	19.492168	0.037088
13	<i>Tat</i>	-2.451456	0.013747	26	<i>Gm12613</i>	21.880545	0.000115

Table S4. Differentially expressed genes identified by RNA-seq between Rbbp7 depleted group and control group in mice (ranked by adjusted p (padj) value). Threshold: padj<=0.05 & FoldChange>=1.5 or FoldChange <= -1.5.

	Gene.names	FoldChange	padj		Gene.names	FoldChange	padj
1	<i>Gm21304</i>	-52.969104	0.004894	73	<i>Map3k3</i>	-1.882379	0.013558
2	<i>Rbbp7</i>	-12.209241	0.000000	74	<i>Prdx6</i>	-1.876643	0.000005
3	<i>Csrnp3</i>	-8.041018	0.007163	75	<i>Efh2</i>	-1.868912	0.030518
4	<i>Sall3</i>	-7.678287	0.039383	76	<i>Smarcc1</i>	-1.867213	0.002597
5	<i>Obox8</i>	-7.537744	0.029826	77	<i>Tinagl1</i>	-1.866183	0.041870
6	<i>Epn3</i>	-6.197603	0.004673	78	<i>Fam83h</i>	-1.859869	0.044077
7	<i>Tcf4</i>	-5.500898	0.002652	79	<i>Prdx1</i>	-1.845616	0.018787
8	<i>Dppa1</i>	-5.391131	0.004894	80	<i>Sh3bgrl2</i>	-1.808559	0.029562
9	<i>Mbd1</i>	-5.327907	0.034424	81	<i>Smpd1</i>	-1.807038	0.000520
10	<i>Slc22a23</i>	-5.260543	0.004815	82	<i>Uhmk1</i>	-1.764857	0.000081
11	<i>Avil</i>	-5.173581	0.013558	83	<i>Tpm3-rs7</i>	-1.764186	0.000645
12	<i>Igf2</i>	-5.088922	0.014032	84	<i>Cdk2ap1</i>	-1.762440	0.000035
13	<i>Pcnx</i>	-4.990652	0.026280	85	<i>Smpd13a</i>	-1.730856	0.008367
14	<i>Ptpn4</i>	-4.519104	0.035714	86	<i>Dcbld2</i>	-1.716857	0.022434
15	<i>Fam133b</i>	-4.413639	0.024125	87	<i>Usp25</i>	-1.709897	0.045118
16	<i>Enpep</i>	-4.190188	0.000000	88	<i>Ecpas</i>	-1.691110	0.002953
17	<i>Lgals1</i>	-4.151859	0.004219	89	<i>Itgav</i>	-1.684536	0.013425
18	<i>Gnai1</i>	-4.041768	0.005519	90	<i>Wdr48</i>	-1.681016	0.030392
19	<i>Krt18</i>	-3.916171	0.000000	91	<i>Surf4</i>	-1.676637	0.006368
20	<i>Dipk2a</i>	-3.805178	0.017846	92	<i>Mkrn1</i>	-1.663510	0.003045
21	<i>Cpxm1</i>	-3.799901	0.005533	93	<i>Man2a1</i>	-1.654582	0.030518
22	<i>Mid1p1</i>	-3.768777	0.029608	94	<i>Dsp</i>	-1.644744	0.035714
23	<i>Krt7</i>	-3.755746	0.019535	95	<i>Wdr1</i>	-1.639596	0.049088
24	<i>Lgals9</i>	-3.726269	0.017929	96	<i>Larp4b</i>	-1.630630	0.001422
25	<i>Mphosph9</i>	-3.691336	0.017929	97	<i>Lrrfip1</i>	-1.611761	0.045414
26	<i>Fabp3</i>	-3.607500	0.000000	98	<i>Trp53bp2</i>	-1.606328	0.006337
27	<i>Tmem64</i>	-3.580301	0.000000	99	<i>Epcam</i>	-1.597250	0.000506
28	<i>Ugdh</i>	-3.532711	0.018695	100	<i>Kpna3</i>	-1.592466	0.021863
29	<i>Acsbg1</i>	-3.436847	0.024250	101	<i>Kif5b</i>	-1.573044	0.014268
30	<i>Hmgn5</i>	-3.351583	0.000001	102	<i>Lamp2</i>	-1.553099	0.005390
31	<i>Gk</i>	-3.294552	0.004894	103	<i>Gnai2</i>	-1.538865	0.033978
32	<i>Casc4</i>	-3.237080	0.001965	104	<i>Cs</i>	-1.520087	0.004410
33	<i>Oxct1</i>	-3.213495	0.000015	105	<i>Tdrp</i>	-1.512550	0.003345
34	<i>Oasl2</i>	-3.209515	0.040185	106	<i>Gss</i>	-1.507530	0.004894
35	<i>Hkdc1</i>	-3.204702	0.035714	107	<i>Rpl7l1</i>	1.504858	0.002878
36	<i>Krt8</i>	-3.143857	0.000000	108	<i>Btbd18</i>	1.600703	0.047182
37	<i>Neu1</i>	-3.135836	0.000004	109	<i>Mgat3</i>	1.660696	0.018668
38	<i>Aldh1l1</i>	-3.081474	0.028979	110	<i>Nin</i>	1.677819	0.034677
39	<i>Srxn1</i>	-3.051171	0.012077	111	<i>Esrrb</i>	1.724137	0.031575
40	<i>Id2</i>	-3.032006	0.006523	112	<i>Fdft1</i>	1.726739	0.017929
41	<i>Hmox1</i>	-2.977399	0.013558	113	<i>C130074G19Rik</i>	1.736169	0.003475
42	<i>Plekhb2</i>	-2.889412	0.000731	114	<i>Hk1</i>	1.745298	0.013558
43	<i>Sec11a</i>	-2.726497	0.000004	115	<i>Pdrg1</i>	1.802602	0.004219
44	<i>Dab2ip</i>	-2.646504	0.000081	116	<i>Rcc2</i>	1.857586	0.016845
45	<i>Wnt7b</i>	-2.644552	0.022039	117	<i>Gpre5c</i>	2.044058	0.001725
46	<i>Pdcd4</i>	-2.637170	0.017663	118	<i>Gemin4</i>	2.066205	0.036655
47	<i>Serpinb9b</i>	-2.631519	0.000013	119	<i>Fdx1</i>	2.092624	0.020442
48	<i>Atp1b1</i>	-2.567392	0.000031	120	<i>Soes3</i>	2.166859	0.018695
49	<i>Cubn</i>	-2.485688	0.000309	121	<i>Urm1</i>	2.238715	0.002953
50	<i>Zfp367</i>	-2.442021	0.002953	122	<i>Tdpoz2</i>	2.260054	0.033450
51	<i>Apoe</i>	-2.431766	0.030518	123	<i>Nkx6-2</i>	2.295950	0.020442
52	<i>Cep55</i>	-2.429618	0.038685	124	<i>Sec1</i>	2.298934	0.012077
53	<i>Capn2</i>	-2.398755	0.021959	125	<i>Trim43b</i>	2.386413	0.000040
54	<i>Sema4g</i>	-2.391392	0.028979	126	<i>Ttc3</i>	2.422607	0.016365
55	<i>Erbp2</i>	-2.383151	0.006976	127	<i>Arrb1</i>	2.495990	0.032967
56	<i>Lama3</i>	-2.341917	0.039118	128	<i>Sox12</i>	2.533996	0.042322

57	<i>D030056L22Rik</i>	-2.322732	0.005125	129	<i>Trim43c</i>	2.536245	0.000890
58	<i>Sqstm1</i>	-2.280566	0.000001	130	<i>Rnf169</i>	2.581380	0.047182
59	<i>Morf41l</i>	-2.220800	0.000000	131	<i>Ddit4</i>	2.610701	0.000058
60	<i>Vps26a</i>	-2.209144	0.000006	132	<i>Col5a3</i>	2.780061	0.044801
61	<i>Gas6</i>	-2.197632	0.007077	133	<i>Hsd17b1</i>	3.030466	0.013425
62	<i>Lrp2</i>	-2.181080	0.000015	134	<i>Tef</i>	3.364672	0.004592
63	<i>Lima1</i>	-2.178234	0.034424	135	<i>Eng</i>	3.489151	0.004248
64	<i>Lcp1</i>	-2.124731	0.031575	136	<i>Fgf4</i>	4.021575	0.000081
65	<i>9530068E07Rik</i>	-2.097295	0.013425	137	<i>Cers4</i>	4.267109	0.018695
66	<i>Bcor</i>	-2.006322	0.045414	138	<i>Ank2</i>	4.825801	0.002597
67	<i>Cyb5r3</i>	-1.995265	0.008018	139	<i>Pcnt</i>	5.212570	0.000003
68	<i>Rab6a</i>	-1.952622	0.003809	140	<i>Hbs1l</i>	6.681758	0.022039
69	<i>Elovl6</i>	-1.946270	0.000731	141	<i>Cacna1b</i>	8.494671	0.004894
70	<i>Frmd4b</i>	-1.923429	0.039383	142	<i>Mdga1</i>	8.597583	0.001725
71	<i>Rnf38</i>	-1.902923	0.013786	143	<i>Csnk2a3</i>	12.045722	0.000005
72	<i>Palm3</i>	-1.898117	0.017518				

Table S5. Differentially expressed genes identified by RNA-seq between both RBBP4 and 7 depleted group and control group in mice (ranked by adjusted p (padj) value). Threshold: padj<=0.05 & FoldChange>=1.5 or FoldChange <= -1.5.

	Gene.names	FoldChange	padj		Gene.names	FoldChange	padj
1	<i>Pomgnt2</i>	-20.7783348	0.000193	225	<i>Pdrg1</i>	1.93224294	0.000502
2	<i>Btbd6</i>	-19.2075597	0.000350	226	<i>Cbs</i>	1.93250053	0.003040
3	<i>Spcs2</i>	-17.9086065	0.006536	227	<i>Gm9864</i>	1.94442719	0.000005
4	<i>Syngap1</i>	-16.8890522	0.012668	228	<i>Tet1</i>	1.94681121	0.000018
5	<i>Rbbp7</i>	-12.2007993	0.000000	229	<i>Mapkapk3</i>	1.96397255	0.011296
6	<i>Zfp934</i>	-11.861218	0.000312	230	<i>Ddx19b</i>	1.98272316	0.000033
7	<i>Gm2541</i>	-9.97493391	0.017939	231	<i>Rap2a</i>	1.99165917	0.012468
8	<i>Rbbp4</i>	-9.52235835	0.000000	232	<i>Lrrn4</i>	1.99337475	0.036774
9	<i>Rps18-ps3</i>	-8.63705297	0.024221	233	<i>C130026I21Rik</i>	2.01380146	0.011482
10	<i>Susd2</i>	-7.68881107	0.026623	234	<i>Cebpa</i>	2.02699238	0.032577
11	<i>Pcbp4</i>	-7.45443	0.000208	235	<i>Zmat3</i>	2.03257153	0.000009
12	<i>Ecm1</i>	-7.32609007	0.029968	236	<i>Cdc42bpg</i>	2.04406334	0.000260
13	<i>Katnal1</i>	-7.29934007	0.002954	237	<i>Hspb1</i>	2.04935775	0.005132
14	<i>Nckipsd</i>	-6.45602184	0.003467	238	<i>Gm10040</i>	2.05545581	0.006033
15	<i>Slc22a23</i>	-6.30245674	0.000080	239	<i>Ankrd10</i>	2.09915854	0.036697
16	<i>Mbd1</i>	-6.25287164	0.003305	240	<i>Cyb5b</i>	2.10330306	0.003896
17	<i>Spata13</i>	-6.05837976	0.000475	241	<i>Serpine2</i>	2.10383913	0.036725
18	<i>Tcf4</i>	-5.68695458	0.000594	242	<i>Slc27a3</i>	2.11542923	0.035074
19	<i>Caena1h</i>	-5.20497448	0.006771	243	<i>Abhd6</i>	2.12102394	0.012409
20	<i>Irf3</i>	-5.19454564	0.002224	244	<i>Cplane1</i>	2.14974343	0.001905
21	<i>Cpxm1</i>	-5.05791298	0.000019	245	<i>Gata1</i>	2.18054408	0.004445
22	<i>Vtn1</i>	-4.99789092	0.000468	246	<i>Plekhn2</i>	2.18293808	0.010386
23	<i>Gm28439</i>	-4.98187652	0.023536	247	<i>Trim11</i>	2.19790885	0.009481
24	<i>Ptpn4</i>	-4.77949916	0.010298	248	<i>Cmb1</i>	2.20171121	0.036002
25	<i>Syp</i>	-4.76456566	0.003477	249	<i>Sp110</i>	2.20677774	0.003585
26	<i>Plet1</i>	-4.74467588	0.000000	250	<i>Anapc4</i>	2.21095798	0.013906
27	<i>Dmbx1</i>	-4.66900754	0.000969	251	<i>Plekhhg5</i>	2.21947242	0.013409
28	<i>Lars2</i>	-4.42282005	0.004763	252	<i>Ctcl</i>	2.25785116	0.000671
29	<i>Dok1</i>	-4.3707729	0.000019	253	<i>Rev1</i>	2.28167306	0.016077
30	<i>Pik3cd</i>	-4.29939265	0.000620	254	<i>Efna3</i>	2.29854167	0.002815
31	<i>Eif4a-ps4</i>	-4.22506569	0.004621	255	<i>Ccp110</i>	2.29885576	0.018385
32	<i>Id2</i>	-4.21286975	0.000008	256	<i>Btbd18</i>	2.30387279	0.000170
33	<i>Tat</i>	-4.19099987	0.000000	257	<i>Ppp3ca</i>	2.30528977	0.006795
34	<i>Glrx</i>	-4.01346908	0.002007	258	<i>Ptpns</i>	2.3151558	0.029994
35	<i>Kcnab2</i>	-3.95229843	0.023701	259	<i>Tbc1d8</i>	2.35986365	0.016362
36	<i>Wdr47</i>	-3.89064727	0.000475	260	<i>Plk2</i>	2.36940656	0.000609
37	<i>Fhod1</i>	-3.79047368	0.040640	261	<i>Gm38393</i>	2.38436577	0.013906
38	<i>Tmem131l</i>	-3.75182538	0.030029	262	<i>Wnk3</i>	2.39872921	0.002258
39	<i>Kdelr1</i>	-3.71954361	0.000007	263	<i>H1f0</i>	2.39940002	0.016555
40	<i>Hnrnp1</i>	-3.54593397	0.000000	264	<i>Tsen2</i>	2.39965857	0.033675
41	<i>F2r1l</i>	-3.49114586	0.016673	265	<i>H3f3b</i>	2.41682539	0.000000
42	<i>Pak6</i>	-3.43949459	0.025526	266	<i>Cep250</i>	2.42181633	0.013578
43	<i>Fbxo3</i>	-3.42560321	0.000033	267	<i>Csrnp2</i>	2.42348133	0.013987
44	<i>Cdc42ep1</i>	-3.41960309	0.000257	268	<i>Ddit4</i>	2.42434522	0.000124
45	<i>Kif21b</i>	-3.40038205	0.022252	269	<i>Neto2</i>	2.42483228	0.036222
46	<i>Erbb2</i>	-3.34390478	0.000005	270	<i>Ddhd1</i>	2.43188107	0.000170
47	<i>Mfn2</i>	-3.33440044	0.000000	271	<i>2010300C02Rik</i>	2.43630939	0.023701
48	<i>Txndc16</i>	-3.31784456	0.034999	272	<i>Tubb6</i>	2.46489207	0.000208
49	<i>Mfsd13a</i>	-3.28929329	0.001283	273	<i>Tchp</i>	2.47062086	0.011963
50	<i>Flot1</i>	-3.25888802	0.043173	274	<i>Pmaip1</i>	2.48570017	0.000007
51	<i>Nr4a1</i>	-3.25122477	0.001754	275	<i>AC132444.1</i>	2.48771838	0.006795
52	<i>E2f2</i>	-3.23609754	0.000475	276	<i>Ddr2</i>	2.49469036	0.040640
53	<i>Lrfr1</i>	-3.1999459	0.003896	277	<i>Tdpoz2</i>	2.50163807	0.005411
54	<i>Znrd1</i>	-3.199789	0.000370	278	<i>Ptpn21</i>	2.50623697	0.004445
55	<i>Igsf3</i>	-3.19875066	0.001122	279	<i>Def6</i>	2.52416407	0.026727
56	<i>Tbc1d2b</i>	-3.10364818	0.036983	280	<i>Cry1</i>	2.5447563	0.000002

57	<i>Mmache</i>	-3.09034607	0.014356	281	<i>Rdh10</i>	2.54739601	0.000170
58	<i>Bloc1s5</i>	-2.96103292	0.042573	282	<i>Cbx7</i>	2.54935621	0.003896
59	<i>Tmem254b</i>	-2.92250623	0.005786	283	<i>Ergic1</i>	2.59330121	0.010959
60	<i>Atp1b1</i>	-2.9155029	0.000000	284	<i>Nkx6-2</i>	2.60583293	0.001997
61	<i>Mpzl2</i>	-2.84708289	0.000050	285	<i>Slc22a13b</i>	2.6085633	0.023908
62	<i>Pank3</i>	-2.83415604	0.000000	286	<i>Mgarp</i>	2.61370903	0.000333
63	<i>Vangl1</i>	-2.80678882	0.013272	287	<i>Hectd4</i>	2.61831402	0.000033
64	<i>Krt18</i>	-2.79975725	0.000008	288	<i>Inpp1l</i>	2.6285218	0.000041
65	<i>Pik3c2a</i>	-2.79639624	0.000762	289	<i>Btg2</i>	2.63788473	0.000295
66	<i>Tmem106b</i>	-2.79331672	0.041453	290	<i>Rab31</i>	2.64500281	0.013066
67	<i>Dtd2</i>	-2.78579406	0.022002	291	<i>Gadd45b</i>	2.65907788	0.026623
68	<i>Ankrd50</i>	-2.76187711	0.028565	292	<i>Tctn1</i>	2.68823517	0.020971
69	<i>Fmn13</i>	-2.71536522	0.005984	293	<i>Foxe1</i>	2.70522208	0.005786
70	<i>Lin37</i>	-2.71437152	0.014356	294	<i>BC021767</i>	2.71221833	0.005307
71	<i>Tubb5</i>	-2.71233725	0.007908	295	<i>E030030106Rik</i>	2.72640243	0.006250
72	<i>Sac3d1</i>	-2.70626918	0.006113	296	<i>Pcyox1</i>	2.73425037	0.001856
73	<i>Zfp57</i>	-2.69871	0.034416	297	<i>Spred3</i>	2.73661492	0.027376
74	<i>Mtm1</i>	-2.69000753	0.033639	298	<i>Micall1</i>	2.76350318	0.002831
75	<i>Zfp367</i>	-2.68670527	0.000221	299	<i>Zfp326</i>	2.78010198	0.006219
76	<i>2610001J05Rik</i>	-2.67135376	0.013385	300	<i>Akap9</i>	2.79785039	0.041299
77	<i>Smpd1</i>	-2.66386942	0.000000	301	<i>Tmem229b</i>	2.81908688	0.028907
78	<i>Hmgn5</i>	-2.66149956	0.000104	302	<i>Hormad1</i>	2.82372757	0.026623
79	<i>Ptpn3</i>	-2.65194521	0.000076	303	<i>Ina</i>	2.88575329	0.012103
80	<i>Ckap2l</i>	-2.59487877	0.002118	304	<i>Slc25a42</i>	2.89070296	0.002428
81	<i>Ugp2</i>	-2.58582393	0.000170	305	<i>Gm14401</i>	2.91338268	0.026623
82	<i>Naga</i>	-2.57095322	0.002388	306	<i>Ddit4l</i>	3.010798	0.000065
83	<i>Pafah1b2</i>	-2.54365102	0.000000	307	<i>Slc16a6</i>	3.02132448	0.000008
84	<i>Plk3</i>	-2.51950323	0.009537	308	<i>Lrp1</i>	3.02521593	0.010874
85	<i>Fabp3</i>	-2.50822624	0.000000	309	<i>Qpctl</i>	3.03573476	0.010509
86	<i>Kpna2</i>	-2.49986966	0.000000	310	<i>S1pr2</i>	3.03721389	0.004749
87	<i>Dab2ip</i>	-2.48691805	0.000161	311	<i>Dcbl2</i>	3.04777762	0.000000
88	<i>Serpib9b</i>	-2.47949391	0.000026	312	<i>Akl</i>	3.05230838	0.018852
89	<i>Prss8</i>	-2.47303969	0.010505	313	<i>Snrk</i>	3.06729272	0.009550
90	<i>Cdca3</i>	-2.43850898	0.000002	314	<i>Epm2aip1</i>	3.09342315	0.000010
91	<i>Efh2</i>	-2.42702836	0.000475	315	<i>Evisl</i>	3.10058578	0.043077
92	<i>Lmna</i>	-2.41378235	0.000316	316	<i>Rnf169</i>	3.12406045	0.002893
93	<i>Mob1a</i>	-2.40997734	0.000000	317	<i>Lgals9</i>	3.14305452	0.024626
94	<i>Kif16b</i>	-2.39059906	0.000651	318	<i>Ptpn14</i>	3.22849468	0.003390
95	<i>Nelfb</i>	-2.38967616	0.005043	319	<i>Col9a2</i>	3.23675648	0.000000
96	<i>Cep55</i>	-2.37760168	0.023536	320	<i>Thyn1</i>	3.2647806	0.005536
97	<i>St6galnac2</i>	-2.37450001	0.000193	321	<i>Nectin4</i>	3.26494939	0.022565
98	<i>Nusap1</i>	-2.37152223	0.033037	322	<i>Slc37a2</i>	3.27620949	0.000370
99	<i>Usp16</i>	-2.3492201	0.000015	323	<i>Nefh</i>	3.29121656	0.016537
100	<i>Lama3</i>	-2.33457335	0.020164	324	<i>Cdh3</i>	3.30855249	0.003768
101	<i>Zfp180</i>	-2.30816697	0.027661	325	<i>P2rx7</i>	3.30886548	0.000178
102	<i>Pif1</i>	-2.2946626	0.044253	326	<i>Zhx3</i>	3.31261762	0.005411
103	<i>Dsg2</i>	-2.29365924	0.041299	327	<i>Gm4779</i>	3.3152004	0.005373
104	<i>Tmem79</i>	-2.28053353	0.032628	328	<i>Cpne1</i>	3.32459929	0.002224
105	<i>Trp53bp2</i>	-2.27396955	0.000002	329	<i>Col5a3</i>	3.35917781	0.002793
106	<i>Dlg3</i>	-2.25917659	0.035393	330	<i>Parp12</i>	3.37381287	0.036776
107	<i>Myo18a</i>	-2.25906694	0.035393	331	<i>Slc44a2</i>	3.3763413	0.006121
108	<i>Wdr1</i>	-2.25117327	0.000475	332	<i>Agpat4</i>	3.37983328	0.032628
109	<i>Prr11</i>	-2.24936925	0.008685	333	<i>Pgap1</i>	3.38390372	0.000003
110	<i>Casc4</i>	-2.24223838	0.041453	334	<i>Map3k20</i>	3.40461913	0.001468
111	<i>Ncapd2</i>	-2.23772026	0.000026	335	<i>Cobl1l</i>	3.42155831	0.000908
112	<i>Pdcd4</i>	-2.20389172	0.039065	336	<i>Ube2r2</i>	3.4286652	0.000906
113	<i>Ptprn</i>	-2.18638697	0.016083	337	<i>Itgb4</i>	3.46080592	0.009085
114	<i>Enpep</i>	-2.17572868	0.000028	338	<i>Pramef17</i>	3.47140035	0.006671
115	<i>Clic4</i>	-2.16638365	0.000001	339	<i>Hspa1b</i>	3.47521578	0.000370
116	<i>Gtpbp1</i>	-2.12997606	0.012007	340	<i>Nsmaf</i>	3.47611275	0.000000
117	<i>Tinagl1</i>	-2.12631794	0.005455	341	<i>Prx</i>	3.49641987	0.040640
118	<i>Ppp1ccb</i>	-2.1031986	0.015957	342	<i>Tmem63a</i>	3.50212056	0.037805

119	<i>Cdx2</i>	-2.09968928	0.005786	343	<i>Syt11</i>	3.5997837	0.022002
120	<i>Mki67</i>	-2.09315668	0.001304	344	<i>Adap1</i>	3.62219463	0.003278
121	<i>Tanc1</i>	-2.08755268	0.010760	345	<i>Gm5662</i>	3.63113518	0.011630
122	<i>Itga5</i>	-2.08321353	0.044796	346	<i>Serinc5</i>	3.63799477	0.000161
123	<i>Max</i>	-2.06917403	0.000031	347	<i>Mettl7a3</i>	3.65042188	0.018145
124	<i>Nkiras2</i>	-2.04041011	0.009268	348	<i>Hlf10</i>	3.65457595	0.034241
125	<i>Tmem254c</i>	-2.03229263	0.014452	349	<i>Azin2</i>	3.65505247	0.020121
126	<i>Cyb5r3</i>	-2.02776085	0.003014	350	<i>AC125149.3</i>	3.66874564	0.000002
127	<i>Mtf2</i>	-2.02614442	0.000000	351	<i>Sycp1</i>	3.68572145	0.000620
128	<i>Gabarap</i>	-1.99237693	0.005786	352	<i>Cercam</i>	3.7008603	0.040016
129	<i>Taf6l</i>	-1.98814697	0.041299	353	<i>B3gnt1</i>	3.70265173	0.009500
130	<i>Slc35f6</i>	-1.96869803	0.023621	354	<i>Arrdc3</i>	3.74590596	0.000021
131	<i>Smc6</i>	-1.94702746	0.006795	355	<i>Mrgprc2-ps</i>	3.77399489	0.005132
132	<i>Smtn</i>	-1.93773149	0.033675	356	<i>Cd81</i>	3.78932659	0.000057
133	<i>Nynrin</i>	-1.93490412	0.007678	357	<i>Hpcal1</i>	3.80819453	0.002815
134	<i>Akr1b8</i>	-1.92755881	0.020553	358	<i>Sec1</i>	3.82899048	0.000000
135	<i>Mtmr4</i>	-1.91623472	0.002810	359	<i>Pcnt</i>	3.84065033	0.001163
136	<i>Ube2m</i>	-1.90490799	0.000076	360	<i>H2bc4</i>	3.87529959	0.047525
137	<i>Chfr</i>	-1.89706091	0.036776	361	<i>Gm12183</i>	3.95101947	0.018852
138	<i>Csf3r</i>	-1.89458848	0.000802	362	<i>Kctd15</i>	3.99868323	0.036776
139	<i>Zc3h3</i>	-1.89161915	0.023621	363	<i>Fhl2</i>	4.04697325	0.027311
140	<i>Shroom3</i>	-1.83965585	0.034369	364	<i>Klrg2</i>	4.07182514	0.000539
141	<i>Ptges</i>	-1.83145072	0.000030	365	<i>Gm28036</i>	4.07482622	0.001311
142	<i>Prkcsb</i>	-1.82702924	0.003896	366	<i>Srl</i>	4.07636621	0.002101
143	<i>Arid3b</i>	-1.82554074	0.039797	367	<i>Ciita</i>	4.07900923	0.002037
144	<i>Rnf185</i>	-1.82455698	0.020900	368	<i>H2aw</i>	4.08919196	0.001849
145	<i>Vps50</i>	-1.82289395	0.010095	369	<i>Klhdc7a</i>	4.11290102	0.000000
146	<i>Gab1</i>	-1.81417637	0.005263	370	<i>Bglap3</i>	4.13303887	0.000001
147	<i>Patl1</i>	-1.81387209	0.011482	371	<i>Acad10</i>	4.14068008	0.000005
148	<i>Acadyl</i>	-1.79769781	0.013359	372	<i>Gm13988</i>	4.16975388	0.000001
149	<i>Mis12</i>	-1.79348853	0.030203	373	<i>Ldha</i>	4.17606089	0.000000
150	<i>Pxk</i>	-1.79181431	0.041998	374	<i>Taok3</i>	4.17660771	0.007041
151	<i>Pttg1</i>	-1.78655341	0.013110	375	<i>4933427I04Rik</i>	4.23207693	0.000000
152	<i>Lmo7</i>	-1.74425333	0.036776	376	<i>Hspa1a</i>	4.26455252	0.003164
153	<i>Klf6</i>	-1.72881061	0.011536	377	<i>Gdpd1</i>	4.38162795	0.018756
154	<i>Ppp1r11</i>	-1.71912217	0.034137	378	<i>Limch1</i>	4.39448362	0.023618
155	<i>Zc3h7a</i>	-1.71004222	0.023701	379	<i>Cd209c</i>	4.50179724	0.000000
156	<i>Agpat2</i>	-1.70928374	0.007434	380	<i>Tex15</i>	4.52118687	0.010874
157	<i>Till12</i>	-1.69727791	0.004445	381	<i>Uchl1</i>	4.56470836	0.000000
158	<i>Vac14</i>	-1.69364045	0.036697	382	<i>Nfam1</i>	4.60338499	0.003454
159	<i>Racgap1</i>	-1.6905866	0.021843	383	<i>Gm11331</i>	4.61081417	0.000000
160	<i>Osbpl7</i>	-1.68721863	0.027993	384	<i>Dusp1</i>	4.64101791	0.000001
161	<i>Depdc7</i>	-1.68630504	0.028083	385	<i>Rgn</i>	4.65728807	0.019100
162	<i>9530068E07Rik</i>	-1.6764872	0.043173	386	<i>H60b</i>	4.66160458	0.000370
163	<i>Strip1</i>	-1.66622677	0.030286	387	<i>Cd1d1</i>	4.66174217	0.000553
164	<i>Net1</i>	-1.66342364	0.006527	388	<i>S100a6</i>	4.69654354	0.023618
165	<i>Dusp4</i>	-1.66200208	0.016537	389	<i>Plekhg1</i>	4.71289638	0.049851
166	<i>Ptpn12</i>	-1.65998641	0.011885	390	<i>Tuba3a</i>	4.75308334	0.011081
167	<i>Tollip</i>	-1.65076648	0.002831	391	<i>Foxb2</i>	4.76129865	0.005132
168	<i>Stard10</i>	-1.64221086	0.000584	392	<i>Prr18</i>	4.78976713	0.022473
169	<i>Ctdspl2</i>	-1.63157472	0.005819	393	<i>Fbxo10</i>	4.79475619	0.043199
170	<i>Bmyc</i>	-1.62291885	0.011760	394	<i>H2-Eb1</i>	4.79752302	0.002246
171	<i>Dap</i>	-1.61310682	0.004476	395	<i>Rhov</i>	4.90935451	0.000403
172	<i>Dlc1</i>	-1.61262302	0.034308	396	<i>Plek2</i>	4.91713317	0.005164
173	<i>Fbxo5</i>	-1.60739502	0.025204	397	<i>Mtcl1</i>	4.96341938	0.016553
174	<i>Trim28</i>	-1.60415949	0.000000	398	<i>Wipil</i>	4.98284934	0.015957
175	<i>Mt2</i>	-1.5942789	0.001856	399	<i>Tef</i>	5.12896337	0.000000
176	<i>St6galnac4</i>	-1.58815077	0.037805	400	<i>Vav1</i>	5.14445417	0.000001
177	<i>Palm3</i>	-1.58503968	0.038396	401	<i>Rasa4</i>	5.18642656	0.000047
178	<i>Tmem231</i>	-1.58298781	0.004081	402	<i>Twsg1</i>	5.24456956	0.000185
179	<i>Osbpl8</i>	-1.5791924	0.006593	403	<i>Eng</i>	5.28436297	0.000000
180	<i>Surf4</i>	-1.57822771	0.005786	404	<i>Lmod3</i>	5.28987181	0.023932

181	<i>Cenpa</i>	-1.57631757	0.020664	405	<i>Ccdc125</i>	5.31000747	0.042856
182	<i>Kpna3</i>	-1.57349153	0.011626	406	<i>Plau</i>	5.3105284	0.000000
183	<i>Vps26a</i>	-1.57117602	0.002810	407	<i>Foxl2</i>	5.51015316	0.038779
184	<i>Srrt</i>	-1.56452235	0.022830	408	<i>Pgbd5</i>	5.53741136	0.004749
185	<i>Krt8</i>	-1.56173569	0.014979	409	<i>Oas1e</i>	5.53983877	0.000015
186	<i>Ptbp3</i>	-1.55896765	0.002376	410	<i>Stox1</i>	5.58732543	0.027311
187	<i>Mef2d</i>	-1.55604896	0.011296	411	<i>Gpx3</i>	5.6034883	0.017253
188	<i>Rnf213</i>	-1.55493279	0.002212	412	<i>Sox9</i>	5.65447335	0.000007
189	<i>Btrc</i>	-1.54831566	0.000078	413	<i>Robo3</i>	5.66268635	0.017506
190	<i>Ripor1</i>	-1.53564143	0.025577	414	<i>Hbs1l</i>	5.72044444	0.040115
191	<i>Kank2</i>	1.51847623	0.025239	415	<i>Eif4e1b</i>	5.74203697	0.000010
192	<i>Tmem63b</i>	1.54570703	0.035741	416	<i>Tmc7</i>	5.76309554	0.033675
193	<i>Man2b1</i>	1.57555436	0.037805	417	<i>Il34</i>	5.83925948	0.017373
194	<i>Stard4</i>	1.5763815	0.002058	418	<i>Synm</i>	6.00513511	0.000423
195	<i>Timm29</i>	1.60361201	0.040161	419	<i>Bbs7</i>	6.02309765	0.000008
196	<i>Sirt1</i>	1.6043537	0.002723	420	<i>Foxq1</i>	6.12685042	0.047602
197	<i>Mdm2</i>	1.61031631	0.000685	421	<i>Slc4a8</i>	6.14678348	0.000072
198	<i>Slc66a2</i>	1.61386611	0.023618	422	<i>Trim7</i>	6.1502463	0.001736
199	<i>Fdft1</i>	1.62479404	0.014402	423	<i>Sema6a</i>	6.1624148	0.000769
200	<i>Ric1</i>	1.62518782	0.036776	424	<i>Txnip</i>	6.16755946	0.018892
201	<i>Dhx32</i>	1.64766927	0.007718	425	<i>Ptafr</i>	6.18849072	0.028565
202	<i>Cadm1</i>	1.6553278	0.014903	426	<i>Pnma2</i>	6.21314343	0.001036
203	<i>Nin</i>	1.66736196	0.017555	427	<i>Mgl2</i>	6.29813999	0.000001
204	<i>Acad11</i>	1.67909196	0.027933	428	<i>Garnl3</i>	6.33858737	0.013279
205	<i>Vav2</i>	1.72587592	0.005278	429	<i>BC051019</i>	6.82571542	0.000000
206	<i>Wdr35</i>	1.72629146	0.018949	430	<i>Sall3</i>	6.88282377	0.006016
207	<i>Myo9b</i>	1.72821999	0.017024	431	<i>Dop1b</i>	6.9955999	0.037805
208	<i>Smcr8</i>	1.73015862	0.009700	432	<i>Cdhr2</i>	7.11228903	0.000137
209	<i>Ccdc117</i>	1.73323542	0.000196	433	<i>Klrb1a</i>	7.21229102	0.028565
210	<i>Zfp239</i>	1.73405942	0.023932	434	<i>Tekt2</i>	7.32568282	0.041299
211	<i>Rbsn</i>	1.75601834	0.012616	435	<i>Peg10</i>	7.53443929	0.005094
212	<i>Trp53bp1</i>	1.7631879	0.023273	436	<i>Acvrl1</i>	8.08506545	0.020869
213	<i>Ryr1</i>	1.76425522	0.010959	437	<i>Adcy5</i>	8.14108578	0.000026
214	<i>Psg16</i>	1.77995647	0.004168	438	<i>Krt19</i>	8.85540902	0.000000
215	<i>AA467197</i>	1.79013578	0.013066	439	<i>Csnk2a3</i>	9.84790008	0.000294
216	<i>Rbm38</i>	1.82882873	0.010874	440	<i>Gabrr1</i>	10.7204597	0.032628
217	<i>Ing1</i>	1.8456153	0.032577	441	<i>Elovl3</i>	13.4286338	0.000000
218	<i>Urm1</i>	1.84733961	0.012329	442	<i>Arhgap33</i>	18.2747841	0.008108
219	<i>Cdc7</i>	1.85895242	0.017129	443	<i>Vcan</i>	18.3132705	0.006677
220	<i>Resf1</i>	1.88145306	0.001856	444	<i>Cd247</i>	19.3238317	0.002237
221	<i>Phlda3</i>	1.91990025	0.003503	445	<i>Tusc3</i>	22.0708717	0.000350
222	<i>Cth</i>	1.92579998	0.000741	446	<i>Gm12613</i>	24.3199762	0.000001
223	<i>Klhl22</i>	1.92663738	0.039065	447	<i>Rsc1a1</i>	47.793453	0.006881
224	<i>I0C0044D17Rik</i>	1.92766068	0.038255				