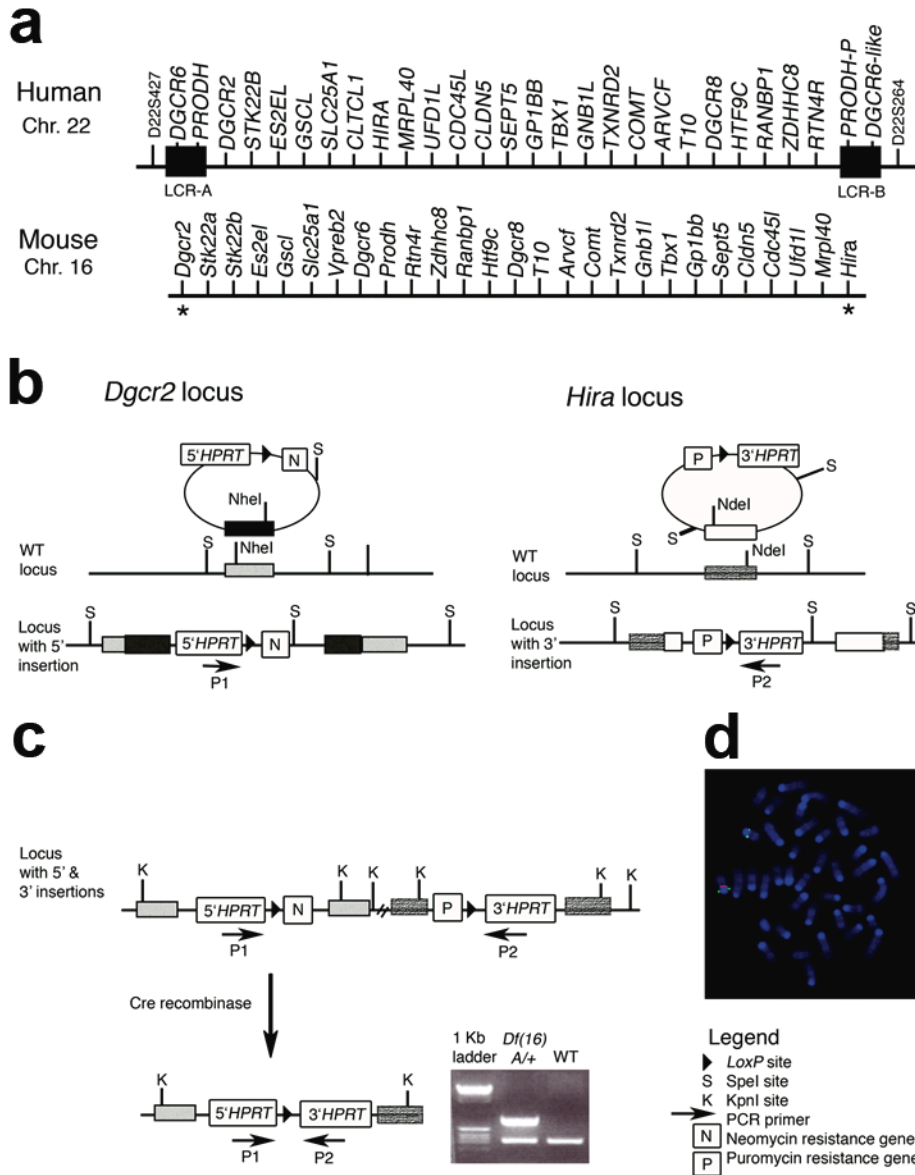


SUPPLEMENTARY INFORMATION FOR

**Altered brain microRNA biogenesis in mice deficient for the 22q11 region
contributes to behavioral and neuronal deficits**

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Supplementary Figure 1: Generation of *Df(16)A*^{+/-} mice.

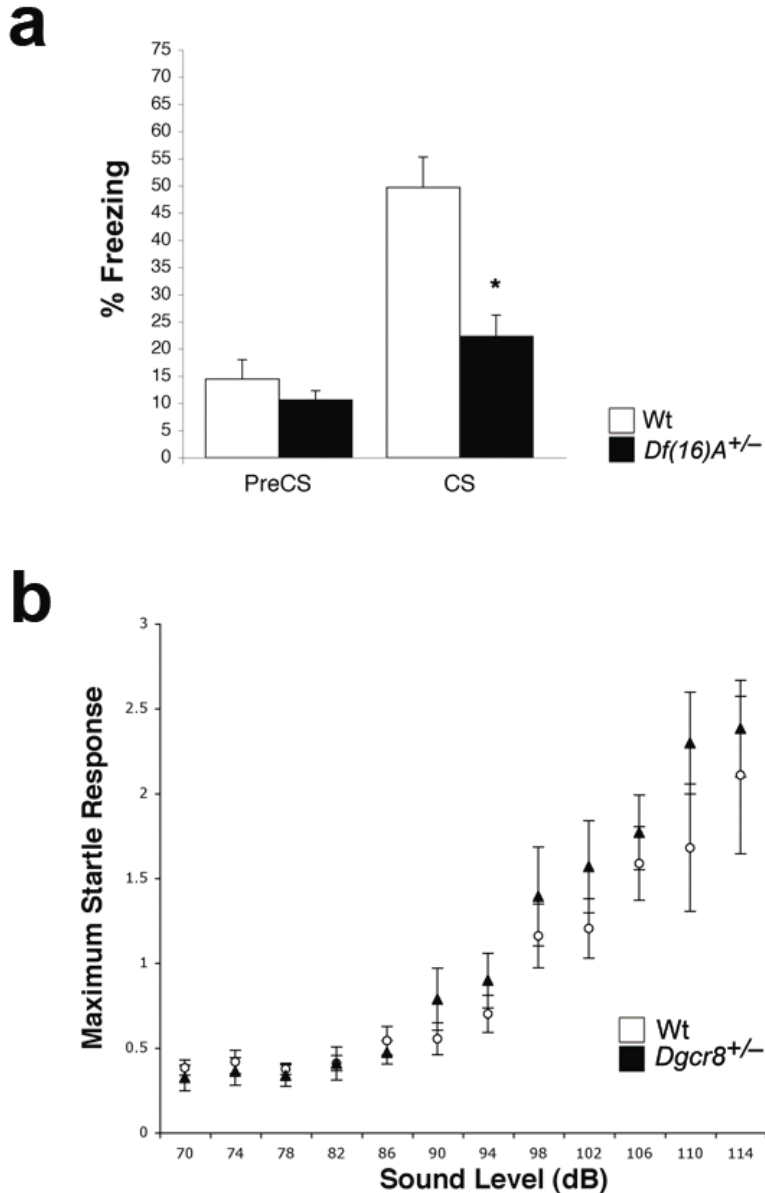
(A) Schematic diagram showing the human chromosome 22q11.2 region, located between microsatellite markers D22S427 and D22S264, and the syntenic mouse region. Almost all of the functional human genes in this segment are represented in the mouse, organized in a slightly different order¹. The 1.5-Mb deletion is mediated by low copy repeat sequences LCR-A and LCR-B (illustrated as black boxes). *PRODH-P* and *DGCR6-like* indicate pseudogenes. *Dgcr2* and *Hira*, the two endpoints of the targeted deletion, are indicated by asterisks.

(B) WT *Dgcr2* and *Hira* loci and the corresponding targeted loci following introduction of a 5'HPRT mini-cassette and a 3'HPRT mini-cassette, respectively.

(C) Cre-induced recombination between *loxP* sites *in cis* leads to the generation of a functional *HPRT* minigene and a 1.3-Mb deficiency in mice. Due to the recombination of the *loxP* sites, a diagnostic 829-bp PCR product can be detected in *Df(16)A^{+/-}* mice.

(D) FISH analysis of *Df(16)A^{+/-}* mice. Metaphase preparations from splenocyte cultures demonstrate a HET deletion on mouse chromosome 16. BAC probe RP23-356A24 (green) is located outside the deleted region and BAC probe RP23-55L18 (red) lies within the deleted region. Diagrams are not drawn to scale.

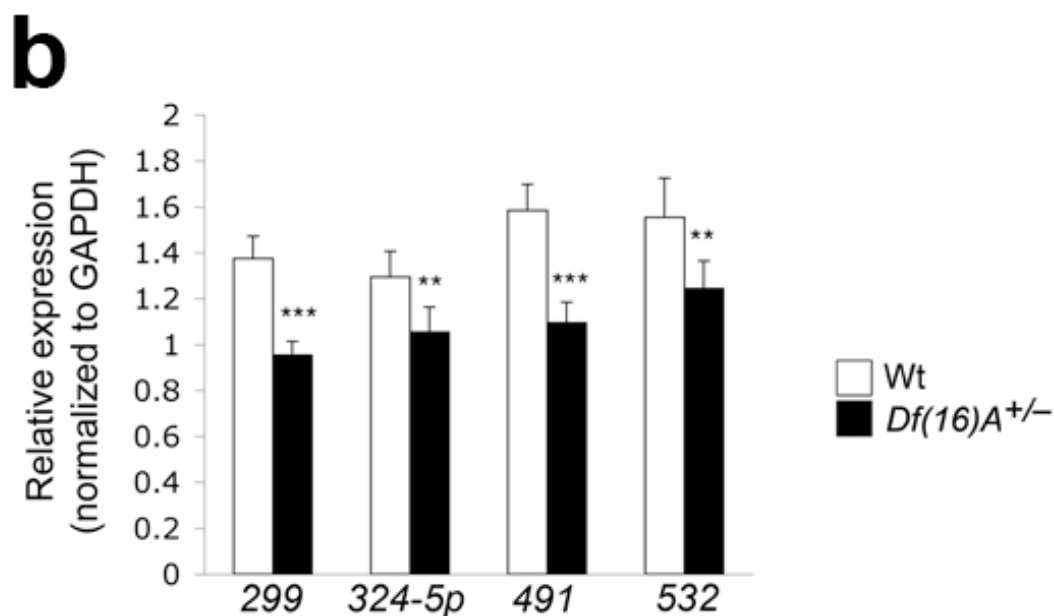
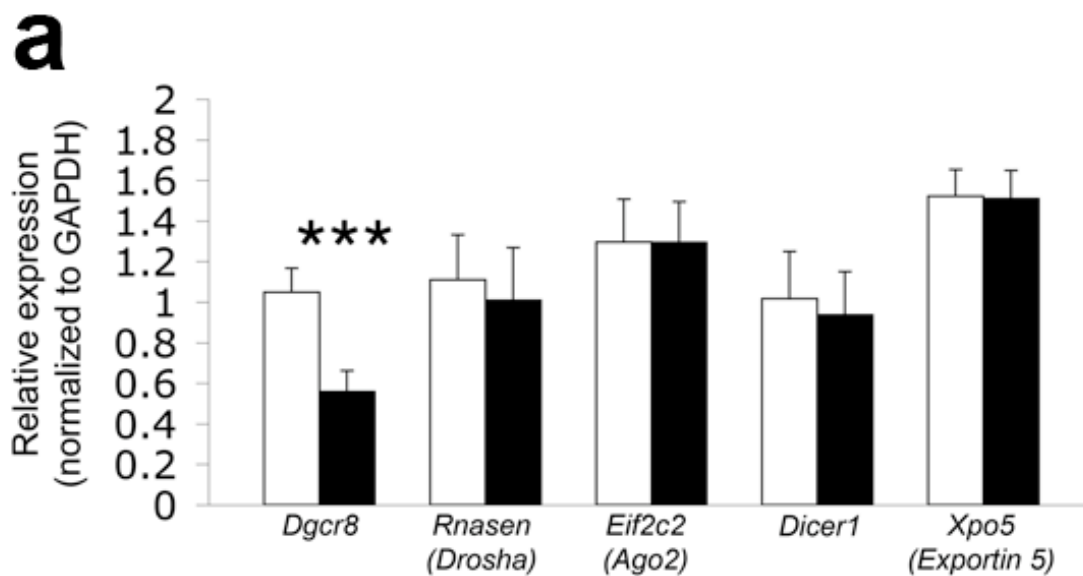
1. Puech, A. et al. Comparative mapping of the human 22q11 chromosomal region and the orthologous region in mice reveals complex changes in gene organization. *Proceedings of the National Academy of Sciences of the United States of America* **94**, 14608-13 (1997).



Supplementary Figure 2. Follow-up behavioral analysis.

(A) An additional cohort of *Df(16)A*^{+/-} mice displays deficits in cued fear conditioning: 10 *Df(16)A*^{+/-} male mice and 10 WT littermate control male mice were exposed to 2 tone-footshock pairings in a conditioning chamber, and then were returned to their home cages. 48 h later, mice were exposed to a novel chamber (PreCS), and no significant differences in % freezing time were found ($P > 0.05$). When presented with the tone (CS), however, *Df(16)A*^{+/-} mice were found to freeze significantly less than WT mice ($P < 0.05$). PreCS: preconditioned stimulus. CS: conditioned stimulus. * $P < 0.05$. Data are shown as mean \pm S.E.M.

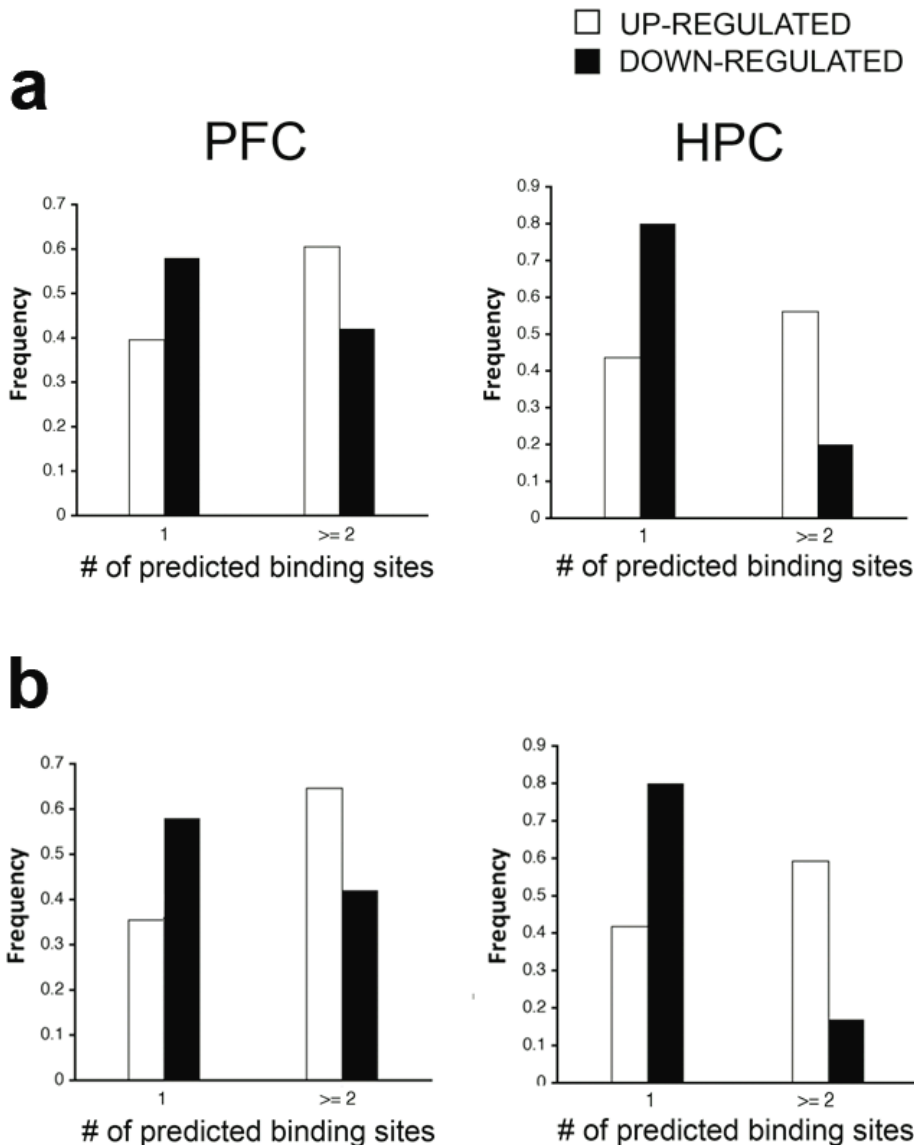
(B) *Dgcr8*^{+/-} mice display normal hearing: Startle response curve session for the *Dgcr8*^{+/-} mice included recordings made every 4 dBs above background (70 dB), up to 114 dBs.



Supplementary Figure 3. Follow-up expression analysis.

(A) Expression analysis of 5 genes [*Dgcr8*, *Rnasen (Drosha)*, *Eif2c2 (Ago2)*, *Dicer1* and *Xpo5 (Exportin5)*] in the miRNA bioprocessing pathway, at the PFC of *Df(16)A*^{+/-} mice. ****P* < 0.001. Data are shown as mean ± S.E.M.

(B) Expression of mature forms of *mir-299*, *mir-324-5p*, *mir-491* and *mir-532* in the PFC of *Df(16)A*^{+/-} mice and WT littermate controls, as assayed by qRT-PCR. Data are shown as mean ± S.E.M. ***P* < 0.01, ****P* < 0.001.



Supplementary Figure 4. Frequency distribution of the miRNA seed sites.

Frequency distribution of the miRNA seed sites at the 3'-UTR of significantly up-regulated and down-regulated transcripts, at the PFC and HPC of *Df(16)A^{+/-}* mice. Note that relative enrichment is exclusively confined in up-regulated PFC and HPC transcripts containing multiple (≥ 2) seed sites. Analysis included GeneChip transcripts annotated in the TargetScan¹ (A) or PicTar² (B) database, which are differentially expressed in the PFC ($n = 710$, FDR P -value < 0.05 ; 210 up-regulated and 500 down-regulated) or HPC ($n = 398$, FDR P -value < 0.05 ; 325 up-regulated and 73 down-regulated).

1. Lewis, B.P., Shih, I.H., Jones-Rhoades, M.W., Bartel, D.P. & Burge, C.B. Prediction of mammalian microRNA targets. *Cell* **115**, 787-98 (2003).
2. Krek, A. et al. Combinatorial microRNA target predictions. *Nature Genetics* **37**, 495-500 (2005).

Supplementary Table 1. List of differentially expressed probe sets in the PFC and HPC of *Df(16)A^{+/-}* mice (FDR *P*-value < 0.01).

Probe_ID	FDR <i>P</i> -value	Rank	Regulation	Gene Symbol	Chr
PFC					
1448900_at	1.5E-13	0	down	D16H22S680E	chr16
1452434_s_at	9.6E-12	2	down	Dgcr6	chr16
1421810_at	9.6E-12	1	down	Dgcr2	chr16
1422547_at	3.2E-11	3	down	Ranbp1	chr16
1449183_at	4.8E-11	5	down	Comt	chr16
1448849_at	4.8E-11	4	down	Mrpl40	chr16
1428190_at	4.8E-11	6	down	Slc25a1	chr16
1419732_at	1.2E-10	7	down	Rtn4r	chr16
1418087_at	3.0E-10	8	down	Ufd1l	chr16
1452357_at	6.5E-10	9	down	Gp1bb///Sept5	chr16
1436468_at	1.4E-09	10	down	Zdhhc8	chr16
1422977_at	5.5E-09	11	down	Gp1bb	chr16
1432367_a_at	2.4E-08	12	down	Ufd1l	chr16
1434730_at	2.1E-07	13	up	Al854517	chr7
1418701_at	2.1E-07	14	down	Comt	chr16
1460033_at	2.2E-07	16	up	C030002C11Rik	chr1
1440357_at	2.2E-07	17	up		chr15
1435439_at	2.2E-07	18	down	Dgcr8	chr16
1416822_at	2.2E-07	15	down	Es2el	chr16
1428753_a_at	3.5E-07	19	down	Dgcr6	chr16
1428562_at	3.6E-07	20	up	2210403K04Rik	chr11
1457030_at	3.6E-07	21	up	Mirg	chr12
1441391_at	1.5E-06	22	down	Gnb1l	chr16
1435179_at	2.4E-06	23	up	C130071C03Rik	chr13
1448115_at	5.7E-06	24	down	Htf9c	chr16
1417629_at	1.0E-05	25	down	Prodh	chr16
1435089_at	1.4E-05	26	up	2010111I01Rik	chr13
1436241_s_at	1.7E-05	27	down	Hira	chr16
1455326_at	1.7E-05	29	up	4932416N17Rik	chr16
1424038_a_at	1.7E-05	28	up	2310044H10Rik	chr7
1431126_a_at	1.9E-05	30	down	0610011F06Rik	chr17
1416821_at	1.9E-05	31	down	Es2el	chr16
1448114_a_at	2.4E-05	33	down	Htf9c	chr16
1429972_s_at	2.4E-05	35	down	Txnrd2	chr16
1421809_at	2.4E-05	34	down	Dgcr2	chr16
1417839_at	2.4E-05	32	down	Cldn5	chr16
1416090_at	2.5E-05	36	down	Pdhb	chr1
1416485_at	2.8E-05	37	down	Timm23	chr10
1451000_at	3.2E-05	38	down	1810020E01Rik	chr7
1449097_at	3.4E-05	39	down	Txnrd2	chr16
1431665_a_at	3.6E-05	40	down	Timm8b	chr9
1450855_at	4.6E-05	41	down	Arvcf	chr16
1417052_at	5.7E-05	42	down	Psmb3	chr11

1416910_at	6.1E-05	43	down	Dnajc15	chr14
1439541_at	6.2E-05	44	down	4930414L22Rik	chr6
1457675_at	7.0E-05	45	down	2510002D24Rik	chr16
1416810_at	7.2E-05	46	down	Mea1	chr17
1415744_at	7.2E-05	47	down	H2-Ke2	chr17
1439305_at	7.3E-05	48	up		chrX
1423211_at	8.0E-05	49	down	Nola3	chr2
1452591_a_at	1.0E-04	50	down	2410018G20Rik	chr16
1431614_at	1.1E-04	51	up	2810049E08Rik	
1417681_at	1.3E-04	52	down	Nudt21	chr3
1451005_at	1.4E-04	53	down	Sumo1	chr1
1418292_at	1.4E-04	54	down	Asna1	chr8
1434646_s_at	1.5E-04	55	down	Sap18	chr8
1455311_at	1.5E-04	56	down	Dgcr8	chr16
1419812_s_at	1.5E-04	57	down	D11Ert99e	chr11
1423220_at	1.6E-04	58	down	Eif4e	chr3
1434356_a_at	1.6E-04	59	down	Psma5	chr3
1418319_at	1.6E-04	60	down	1810047C23Rik	chr8
1448206_at	1.6E-04	61	down	Psma2	chr13
1417144_at	1.7E-04	62	down	Tubg1	chr11
1437125_at	1.7E-04	63	up	Camk2a	chr18
1436042_at	1.9E-04	64	down	Tln1	chr4
1428764_at	2.1E-04	65	up	Gtl2	chr12
1415741_at	2.1E-04	66	down	Tparl	chr5
1455172_at	2.2E-04	68	down	AU020094	chr14
1448808_a_at	2.2E-04	67	down	Nme2	chr10
1448461_a_at	2.3E-04	69	down	1500006O09Rik	chr14
1433535_x_at	2.3E-04	70	down	Cct2	chr10
1423666_s_at	2.4E-04	71	down	Rpl5	chr1
1415675_at	2.4E-04	72	down	Dpm2	chr2
1444077_at	2.6E-04	73	down		
1451331_at	2.9E-04	74	up	Ppp1r1b	chr11
1427886_at	3.0E-04	75	up	Pom121	chr5
1456685_at	3.1E-04	76	down	Nsg2	chr11
1452047_at	3.1E-04	77	down	Cacybp	chr1
1426541_a_at	3.3E-04	79	up	2310067E08Rik	chr9
1416023_at	3.3E-04	78	down	Fabp3	chr4
1438403_s_at	3.6E-04	80	up	BC003324	chr19
1423281_at	3.6E-04	81	down	Stmn2	chr3
1417258_at	3.7E-04	82	down	Cct5	chr15
1428580_at	3.7E-04	83	down	Blvra	chr2
1442650_at	3.7E-04	84	up		chr3
1452692_a_at	3.8E-04	85	down	Ndufv2	chr17
1460209_at	3.9E-04	86	down	Usp39	chr6
1451230_a_at	3.9E-04	87	down	Wbp5	chrX
1460165_at	3.9E-04	88	down	Ppp1ca	chr19
1436383_at	3.9E-04	89	up	Cplx2	chr13
1433670_at	3.9E-04	90	down	Emp2	chr16
1417316_at	3.9E-04	91	down	Them2	chr13

1437704_at	4.0E-04	92	down		chr13
1449362_a_at	4.0E-04	93	up	Mink1	chr11
1460698_a_at	4.2E-04	94	down	Sec1113	chr18
1451366_at	4.2E-04	95	down	Cops6	chr5
1417339_a_at	4.6E-04	97	down	Dncl1	chr5
1416037_a_at	4.6E-04	96	down	Cct2	chr10
1452674_a_at	4.7E-04	98	down	Eif3s12	chr7
1434149_at	4.7E-04	100	up	Tcf4	chr18
1419073_at	4.7E-04	99	down	Tmeff2	chr1
1418002_at	5.2E-04	101	down	Higd2a	chr13
1416282_at	5.2E-04	102	down	Psmc3	chr2
1417891_at	5.3E-04	103	down	Spsb3	chr17
1437423_a_at	5.3E-04	104	down	Sra1	chr18
1449622_s_at	5.4E-04	106	down	Atp6ap1	chrX
1448300_at	5.4E-04	105	down	Mgst3	chr1
1424110_a_at	5.6E-04	107	down	Nme1	chr11
1452882_at	5.6E-04	108	down	Pgrmc2	chr3
1433450_at	5.8E-04	109	up	Cdk5r1	chr11
1423908_at	5.9E-04	110	down	Ndufs8	chr19
1418188_a_at	6.0E-04	111	up	Malat1	chr19
1460695_a_at	6.1E-04	112	up	2010111I01Rik	chr13
1433704_s_at	6.2E-04	113	down	Tloc1	chr3
1426256_at	6.6E-04	114	down	Timm17a	chr1
1436134_at	7.2E-04	115	down	Scn2b	chr9
1443790_x_at	7.3E-04	116	down	4930414L22Rik	chr6
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1457040_at	7.5E-04	118	down	Lgi2	chr5
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1423630_at	8.7E-04	131	up	Cygb	chr11
1435488_at	9.0E-04	135	down	C630010D07Rik	chr5
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1429627_at	9.0E-04	136	down	Ppil3	chr1
1423162_s_at	9.0E-04	134	up	Spred1	chr2
1416971_at	9.0E-04	133	down	Cox7a2	chr9
1420368_at	9.3E-04	137	down	Denr	chr5
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1437466_at	9.5E-04	139	down	Alcam	chr16
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1428631_a_at	9.5E-04	140	down	Uqcrc2	chr7
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1441947_x_at	9.7E-04	143	down	BC033915	chr9
1426446_at	9.7E-04	144	up	6430548M08Rik	chr8
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1435231_at	9.8E-04	154	down	Coq4	chr2
1433662_s_at	9.8E-04	153	up	Timp2	chr11
1429896_at	9.8E-04	147	down	5830408B19Rik	chr10
1426762_s_at	9.8E-04	148	down	Aof2	chr4
1423418_at	9.8E-04	150	down	Fdps	chr3
1422464_at	9.8E-04	151	down	Mrpl3	chr9
1417157_at	9.8E-04	152	down	Actr10	chr12
1415962_at	9.8E-04	149	down	Eif3s3	chr15
1435771_at	9.8E-04	155	down	Plcb4	chr2
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1454978_at	1.0E-03	160	up	Ttyh3	chr5
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1427481_a_at	1.0E-03	157	up	Atp1a3	chr7
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1416979_at	1.0E-03	159	down	2510048O06Rik	chr5
1416000_a_at	1.0E-03	158	down	Prdx1	chr4
1457218_at	1.0E-03	166	down	6430510M02Rik	chr2
1454813_at	1.0E-03	172	down	1110017O22Rik	chr7
1454716_x_at	1.0E-03	168	down	Cox5b	chr1
1452680_at	1.0E-03	167	down	Snrpd2	chr7
1451217_a_at	1.0E-03	169	down	Immp1l	chr2
1441959_s_at	1.0E-03	164	down	1200003C05Rik	chr12
1438678_at	1.0E-03	165	down	1500011K16Rik	chr2
1436796_at	1.0E-03	170	down	1110061A14Rik	chr18
1435630_s_at	1.0E-03	163	down	Acat2	
1424828_a_at	1.0E-03	171	down	Fh1	chr1
1421446_at	1.0E-03	174	up	Prkcc	
1419577_at	1.0E-03	173	down	A530089I17Rik	chr10
1436674_at	1.1E-03	176	down	Rap2ip	
1427914_a_at	1.1E-03	175	down	Tceb1	chr1
1435395_s_at	1.1E-03	177	down	Atp5j2	chr5
1448238_at	1.1E-03	178	down	2700060E02Rik	chr3
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1452082_at	1.2E-03	181	up	6430548M08Rik	chr8
1424786_s_at	1.2E-03	182	down	Wdr45	chrX
1420642_a_at	1.2E-03	183	down	2010100O12Rik	chr2
1416604_at	1.2E-03	184	down	Cyc1	chr15
1429264_at	1.2E-03	185	down	C030044B11Rik	chr13
1416313_at	1.3E-03	186	down	Mllt11	chr3
1450049_a_at	1.3E-03	187	down	Hira	chr16
1451049_at	1.3E-03	189	down	Bcap31	chrX
1426373_at	1.3E-03	188	up	Ski	chr4

1428541_at	1.3E-03	190	up	3321401G04Rik	chr6
1425383_a_at	1.3E-03	191	up	Pbx1	chr1
1423737_at	1.3E-03	192	down	Ndufs3	chr2
1448822_at	1.3E-03	193	down	Psemb6	chr11
1444120_at	1.3E-03	194	up	Bin1	chr18
1444291_at	1.4E-03	195	down	4930506D23Rik	chr7
1416669_s_at	1.4E-03	196	down	Naca	chr10
1427878_at	1.4E-03	197	down	0610010O12Rik	chr18
1426371_at	1.4E-03	198	up	Mlstd2	chr7
1435113_x_at	1.4E-03	199	down	Stmn3	
1416834_x_at	1.4E-03	200	down	Ndufb2	chr6
1416668_at	1.4E-03	201	down	4921531G14Rik	chr15
1424001_at	1.4E-03	202	down	Mki67ip	chr1
1417105_at	1.4E-03	203	down	1810017G16Rik	chr8
1428588_a_at	1.4E-03	204	down	Mrpl41	chr2
1435437_at	1.5E-03	205	up		chr3
1449273_at	1.5E-03	206	up	Cyfp2	chr11
1438682_at	1.5E-03	207	up	Pik3r1	chr13
1455574_at	1.5E-03	208	up	9430023P16Rik	chr1
1451385_at	1.5E-03	209	down	2310056P07Rik	chr16
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1418137_at	1.5E-03	211	down	Mrp63	chr14
1453582_at	1.5E-03	213	up	Chka	chr19
1424147_at	1.5E-03	212	down	Ahsa1	chr12
1448368_at	1.5E-03	214	down	Dctn6	chr8
1460729_at	1.5E-03	215	up	Rock1	chr18
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1423728_at	1.6E-03	217	down	Eif3s6ip	chr15
1424665_at	1.6E-03	218	down	5430405G24Rik	chr11
1442913_at	1.6E-03	219	up		
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1453713_s_at	1.6E-03	221	up	4930546H06Rik	chr17
1426761_at	1.6E-03	222	down	Aof2	chr4
1456614_at	1.7E-03	223	down	Acn9	chr6
1434280_at	1.7E-03	224	up		
1455960_at	1.7E-03	226	up	Egfl5	chr4
1452142_at	1.7E-03	228	up	Slc6a1	chr6
1433598_at	1.7E-03	225	up	9430010O03Rik	chr8
1419255_at	1.7E-03	227	up	Spnb2	chr11
1450853_at	1.7E-03	231	down	Tle4	chr19
1450668_s_at	1.7E-03	229	down	Hspe1	chr1
1448465_at	1.7E-03	230	down	Nipsnap1	chr11
1452346_at	1.8E-03	232	down	B3gnt6	chr19
1434053_x_at	1.8E-03	235	down	Atp5k	chr5
1429004_at	1.8E-03	234	down	Phip	chr9
1417077_at	1.8E-03	233	down	Bcap29	chr12
1460198_a_at	1.8E-03	237	down	Psemb3	chr11
1423815_at	1.8E-03	236	down	Ddx56	chr11
1438091_a_at	1.8E-03	239	down	H2afz	chr3

1433955_at	1.8E-03	238	down	Brwd1	chr16
1433460_at	1.9E-03	240	up	Ttc7b	chr12
1449255_a_at	1.9E-03	241	down	Rpl15	chr4
1424412_at	1.9E-03	242	down	Ogfrl1	chr1
1460697_s_at	1.9E-03	245	down	2610209M04Rik	chr6
1449162_at	1.9E-03	244	down	Pop7	chr5
1416902_a_at	1.9E-03	243	down	Cox5b	chr1
1436226_at	2.0E-03	246	down	Tceb1	chr1
1430123_a_at	2.0E-03	247	down	Akr1a4	chr4
1455006_at	2.0E-03	248	down	2310016M24Rik	chr15
1428163_at	2.0E-03	250	down	Sara2	chr11
1416269_at	2.0E-03	249	down	Atp5j2	chr5
1416782_s_at	2.0E-03	251	down	Praf2	chrX
1423181_s_at	2.0E-03	252	down	Clns1a	chr7
1455620_at	2.0E-03	254	down	chr7	
1451205_at	2.0E-03	253	down	Psemb4	chr3
1416478_a_at	2.0E-03	255	down	Mdh2	chr5
1457268_at	2.1E-03	256	up	Dot1l	chr10
1430231_a_at	2.1E-03	257	up	C030018L16Rik	chr9
1448287_at	2.1E-03	259	down	Rpo1-3	chr5
1428463_a_at	2.1E-03	258	up	Ppp2r5e	chr12
1426544_a_at	2.1E-03	260	up	Ttc14	chr3
1428180_at	2.1E-03	261	down	2810422J05Rik	chr8
1437759_at	2.2E-03	262	up	Pitrm1	chr13
1427003_at	2.2E-03	263	down	Ppp2r5c	chr12
1452415_at	2.3E-03	264	up	Actn1	chr12
1456125_a_at	2.3E-03	265	down	Dncl1	chr5
1449505_at	2.3E-03	266	down	Kpna1	chr16
1460237_at	2.3E-03	267	up	Trim8	chr19
1424760_a_at	2.3E-03	268	down	Smyd2	chr1
1438986_x_at	2.3E-03	270	down	Rps17	chr11
1436986_at	2.3E-03	269	up	Sntb2	chr8
1436935_x_at	2.3E-03	271	down	Clns1a	chr7
1427267_at	2.3E-03	272	up	Zfp469	chr5
1434244_x_at	2.3E-03	273	down	Htf9c	chr16
1428406_s_at	2.3E-03	274	down	Hcfc1r1	chr17
1434124_x_at	2.3E-03	275	down	2400001E08Rik	chr7
1449712_s_at	2.4E-03	276	down	Atp6v1e1	chr6
1421027_a_at	2.4E-03	277	up	Mef2c	chr13
1450968_at	2.4E-03	278	down	Uqcrfs1	chr13
1448109_a_at	2.4E-03	282	down	Rpl26	chr5
1439605_at	2.4E-03	280	up		chr6
1428526_at	2.4E-03	281	down	1500034E06Rik	chr11
1418134_at	2.4E-03	279	down	1200007B05Rik	chr18
1429087_at	2.4E-03	283	down	1110054O05Rik	chr4
1425018_at	2.4E-03	284	down	Mcts1	chrX
1417368_s_at	2.4E-03	285	down	Ndufa2	chr18
1435347_at	2.4E-03	286	down	Stau1	chr2
1448319_at	2.5E-03	288	down	LOC432549	chr1

1436780_at	2.5E-03	289	up	Ogt	chrX
1428573_at	2.5E-03	287	down	Chn2	chr6
1423799_at	2.5E-03	290	down	Eif1	chr11
1440816_x_at	2.5E-03	291	down	Ddx1	chr12
1418439_at	2.6E-03	292	down	D10Erttd322e	chr10
1422627_a_at	2.6E-03	293	down	Mkks	chr2
1441960_x_at	2.6E-03	294	down	5730494M16Rik	chr18
1417147_at	2.6E-03	295	down	B230317C12Rik	chr2
1457446_at	2.6E-03	296	up	Opcml	chr9
1436221_at	2.6E-03	297	up	D1Erttd471e	chr1
1450674_at	2.6E-03	298	down	Cdk5	chr5
1427875_a_at	2.7E-03	299	down	1100001I22Rik	chr3
1423266_at	2.7E-03	301	down	2810405K02Rik	chr4
1416853_at	2.7E-03	300	up	Ncdn	chr4
1460195_at	2.7E-03	304	down	Mrps11	chr7
1438289_a_at	2.7E-03	305	down	Sumo1	chr1
1416938_at	2.7E-03	302	down	Chchd1	chr14
1416284_at	2.7E-03	303	down	Mrpl28	chr17
1427432_a_at	2.7E-03	306	down	Sfrs10	chr3
1422733_at	2.7E-03	308	up	Fjx1	chr2
1421375_a_at	2.7E-03	307	down	S100a6	chr3
1437510_x_at	2.7E-03	309	down	Rps17	chr12
1416663_at	2.7E-03	310	down	Ndufa9	chr6
1429192_at	2.8E-03	312	up	Ski	chr4
1427385_s_at	2.8E-03	311	up	Actn1	chr12
1453728_a_at	2.8E-03	313	down	Mrps17	chr5
1423507_a_at	2.8E-03	314	down	Sirt2	chr7
1433700_at	2.8E-03	315	down	4933433P14Rik	chr12
1420632_a_at	2.8E-03	316	down	Bscl2	chr19
1448442_a_at	2.9E-03	322	down	Psma3	chr12
1438889_at	2.9E-03	319	down		chrX
1437801_at	2.9E-03	320	down	Morf4l1	chr9
1425691_at	2.9E-03	318	up	B3gat1	chr9
1420113_s_at	2.9E-03	323	down	2410022L05Rik	chr8
1416963_at	2.9E-03	321	down	Ubadc1	chr2
1416843_at	2.9E-03	317	down	Pde6d	chr1
1422483_a_at	2.9E-03	324	down	Cycs	chr16
1436894_at	2.9E-03	325	up	5330438I03Rik	chr1
1454919_at	2.9E-03	330	down	Nmt2	chr2
1448685_at	2.9E-03	329	down	2900010M23Rik	chr17
1448147_at	2.9E-03	331	up	Tnfrsf19	chr14
1437327_x_at	2.9E-03	326	down	2310057D15Rik	chr5
1435959_at	2.9E-03	328	down	Arhgap15	chr2
1434159_at	2.9E-03	327	up	Stk4	chr2
1460230_at	3.0E-03	333	up	Syn2	chr6
1439095_at	3.0E-03	332	up	Sfrs11	chr3
1416655_at	3.0E-03	334	down	C1galt1c1	chrX
1455248_at	3.0E-03	335	down	0610011N22Rik	chr13
1433625_at	3.1E-03	336	up	5830434P21Rik	chr2

1448212_at	3.1E-03	337	down	Tnfsf5ip1	chr18
1426542_at	3.1E-03	338	up	2310067E08Rik	chr9
1459909_at	3.1E-03	339	up	Nfix	chr8
1451512_s_at	3.1E-03	340	down	Hibch	chr1
1435245_at	3.1E-03	341	down	Gls2	chr10
1434216_a_at	3.1E-03	342	down	Nudt19	chr7
1435246_at	3.1E-03	343	up	Paqr8	chr1
1448122_at	3.1E-03	344	down	Tcp1	chr17
1435364_at	3.1E-03	346	down	Cyhr1	chr2
1416415_a_at	3.1E-03	345	down	H2afz	chr3
1438774_s_at	3.2E-03	347	up	Pgm2l1	chr18
1459563_x_at	3.2E-03	348	up		
1438033_at	3.2E-03	349	up	Tef	chr15
1422442_at	3.2E-03	351	down	Smu1	chr4
1421127_at	3.2E-03	350	down	Tmem42	chr9
1418577_at	3.2E-03	352	up	Trim8	chr19
1417720_at	3.2E-03	353	down	Polr2j	chr5
1456110_at	3.3E-03	354	up	Ankrd11	chr8
1448697_s_at	3.3E-03	355	down	Rpl36al	chr12
1448602_at	3.3E-03	356	up	Pygm	chr19
1416789_at	3.3E-03	357	down	ldh3g	chrX
1437167_at	3.3E-03	359	up	Tmod2	chr9
1421149_a_at	3.3E-03	358	up	Atn1	chr6
1429708_at	3.4E-03	361	down	Ndufa11	chr17
1424539_at	3.4E-03	360	down	Ubl4	chrX
1437524_x_at	3.4E-03	362	down	Coro7	
1448430_a_at	3.4E-03	363	down	Naca	chr10
1422748_at	3.4E-03	364	up	Zfhx1b	chr2
1440097_at	3.4E-03	365	up	Mirg	chr12
1428989_at	3.4E-03	366	down	0710001D07Rik	chr17
1460588_at	3.4E-03	368	down	chr1	
1431145_a_at	3.4E-03	367	down	Cuedc2	chr19
1417035_at	3.4E-03	369	down	Sac3d1	chr19
1450241_a_at	3.4E-03	370	down	Evi2a	chr11
1424740_at	3.4E-03	371	down	Creb3	chr4
1438993_a_at	3.5E-03	372	down	Atp6v1d	chr12
1428468_at	3.5E-03	373	down	3110043O21Rik	chr4
1415972_at	3.5E-03	374	up	Marcks	chr10
1422964_at	3.6E-03	375	down	Rad23a	chr8
1416499_a_at	3.6E-03	376	down	Dctn6	chr8
1417510_at	3.6E-03	377	down	Vps4a	chr8
1448398_s_at	3.6E-03	378	up	Rpl22	chr4
1421122_at	3.6E-03	379	up	Cbll1	chr12
1423538_at	3.6E-03	380	down	Ntan1	chr16
1416045_a_at	3.7E-03	381	down	Smarcb1	chr10
1451569_at	3.7E-03	383	up	Nr2c2	chr6
1448418_s_at	3.7E-03	384	down	Wdr23	chr14
1433449_at	3.7E-03	382	down	B930037P14Rik	chr19
1419414_at	3.8E-03	385	down	Gng13	chr17

1439566_at	3.8E-03	386	up	C030038J10Rik	chr6
1423772_x_at	3.8E-03	387	down	Slc25a5	chr5
1425690_at	3.9E-03	388	up	B3gat1	chr9
1430124_x_at	3.9E-03	389	down	Akr1a4	chr4
1430129_a_at	3.9E-03	390	down	Commd8	chr5
1436850_at	3.9E-03	391	up	Creg2	chr1
1428936_at	3.9E-03	392	up	Atp2b1	chr10
1429610_a_at	3.9E-03	393	down	Zfp511	chr7
1459987_s_at	3.9E-03	398	down	Cct3	chr3
1456137_at	3.9E-03	397	up	Nrxn3	chr12
1452872_at	3.9E-03	394	down	2900054D09Rik	chr10
1438671_at	3.9E-03	395	up	Ppp2r2c	chr5
1426352_s_at	3.9E-03	396	up	Tial1	chr7
1460192_at	3.9E-03	400	down	Osbp1a	chr18
1428201_at	3.9E-03	399	down	2310036O22Rik	chr8
1438193_at	4.0E-03	401	up	Nrxn3	chr12
1422501_s_at	4.0E-03	402	down	ldh3a	chr9
1450694_at	4.0E-03	403	down	Fkbp2	chr19
1434579_x_at	4.0E-03	404	down	Ndufs8	
1435976_at	4.0E-03	405	down		chr4
1455340_at	4.0E-03	407	down	3010003L21Rik	chr6
1448770_a_at	4.0E-03	406	down	Atpif1	chr4
1436455_at	4.0E-03	408	down	Asph	chr4
1441170_a_at	4.1E-03	410	up	Dab2ip	chr2
1416452_at	4.1E-03	409	down	Oat	chr7
1429810_at	4.1E-03	411	up	4921505C17Rik	chr15
1452599_s_at	4.1E-03	412	down	Al413582	chr17
1425265_a_at	4.2E-03	413	down	Prnpip1	chr4
1458114_at	4.2E-03	415	up	Samd12	chr15
1424925_at	4.2E-03	414	down	Sec63	chr10
1417988_at	4.2E-03	416	down	Resp18	chr1
1426565_at	4.2E-03	417	up	Igf1r	chr7
1426543_x_at	4.2E-03	419	up	2310067E08Rik	chr9
1416353_at	4.2E-03	418	down	Nr1h2	chr7
1452285_a_at	4.2E-03	421	down	Eif3s5	chr7
1429918_at	4.2E-03	422	down	Arhgap20	chr9
1424877_a_at	4.2E-03	420	down	Alad	chr4
1425784_a_at	4.3E-03	423	up	Olfm1	chr2
1416508_at	4.3E-03	424	down	Med28	chr5
1456204_at	4.4E-03	426	down	2010107H07Rik	chr14
1435011_x_at	4.4E-03	425	down	Akr1a4	chr4
1451110_at	4.4E-03	427	up	Egln1	chr8
1439940_at	4.4E-03	428	up	2900019G14Rik	chr2
1448959_at	4.4E-03	429	down	Ndufs4	chr13
1449840_at	4.4E-03	430	up	Sntb2	chr8
1422945_a_at	4.5E-03	431	up	Kif5c	chr2
1450467_at	4.5E-03	432	up	Bsn	chr9
1435112_a_at	4.5E-03	433	down	Atp5h	chr11
1428527_at	4.5E-03	435	down	Snx7	chr3

1427665_a_at	4.5E-03	437	up	Nfic	chr10
1425143_a_at	4.5E-03	440	down	Ndufs1	chr1
1424137_at	4.5E-03	438	up	Gprin1	chr13
1423415_at	4.5E-03	434	down	Gpr83	chr9
1421115_a_at	4.5E-03	436	down	Zdhhc16	chr19
1416984_at	4.5E-03	439	down	Mrps18a	chr17
1447919_x_at	4.5E-03	441	down	Ndufab1	chr7
1455044_at	4.5E-03	442	down	Tmem44	chr16
1428257_s_at	4.5E-03	444	down	Dncl2a	chr2
1419743_s_at	4.5E-03	443	down	Carm1	chr9
1444008_at	4.6E-03	445	down	H2afy3	chr10
1439481_at	4.6E-03	446	down	AI845704	chr1
1455420_at	4.7E-03	447	down	Rad23b	chr4
1418212_at	4.7E-03	448	down	Omg	chr11
1419472_s_at	4.7E-03	449	down	Nudc	chr4
1457336_at	4.7E-03	450	up	R3hdm1	chr1
1452705_at	4.7E-03	455	down	AA415817	chr16
1452148_at	4.7E-03	451	down	Lrpap1	chr5
1439436_x_at	4.7E-03	454	down	Incenp	
1421507_at	4.7E-03	452	up	Olfr78	chr7
1418754_at	4.7E-03	453	down	Adcy8	chr15
1416118_at	4.7E-03	456	down		chr3
1440801_s_at	4.7E-03	457	up	Adrbk2	chr5
1435967_s_at	4.7E-03	458	down	Hibadh	chr6
1425587_a_at	4.7E-03	459	up	Ptprij	chr2
1416568_a_at	4.7E-03	460	up	Acin1	chr14
1420934_a_at	4.8E-03	461	up	Srrm1	chr4
1438026_at	4.8E-03	462	down	2310030G09Rik	
1425854_x_at	4.8E-03	465	down	Tcrb-V13	chr6
1423838_s_at	4.8E-03	466	down	2400003C14Rik	chr8
1423150_at	4.8E-03	464	down	Sgne1	chr2
1416360_at	4.8E-03	463	up	Snag1	chr13
1418327_at	4.8E-03	467	down	1110058L19Rik	chr1
1438420_at	4.8E-03	468	up	Rnpc2	chr2
1427955_a_at	4.9E-03	469	down	Deb1	chr9
1423328_at	4.9E-03	470	down	Gdap1	chr1
1416395_at	4.9E-03	471	down	Guk1	chr11
1440516_at	4.9E-03	472	down		chrX
1456892_at	4.9E-03	474	up	D030036P13Rik	chrX
1453314_x_at	4.9E-03	475	down	2610039C10Rik	chr16
1436908_at	4.9E-03	477	down	Pcm1	chr8
1434799_x_at	4.9E-03	476	down	Aldoa	chr7
1432004_a_at	4.9E-03	473	up	Dnm2	chr9
1430529_at	4.9E-03	479	up	Csnk1a1	chr18
1428986_at	4.9E-03	478	up	Slc17a7	chr7
1424441_at	4.9E-03	481	down	Slc27a4	chr2
1423947_at	4.9E-03	482	down	1110008P14Rik	chr2
1418412_at	4.9E-03	483	down	Tpd52l1	chr10
1416556_at	4.9E-03	480	down	Tspan31	chr10

1460196_at	5.0E-03	484	down	Cbr1	chr16
1417913_at	5.0E-03	485	down	2810037C03Rik	chr8
1417128_at	5.0E-03	486	down	2810052M02Rik	chr3
1443863_at	5.0E-03	487	up	Fndc3a	chr14
1454806_at	5.1E-03	488	up	D12ErtD553e	chr12
1428322_a_at	5.1E-03	489	down	Ndufb10	chr17
1437131_x_at	5.1E-03	490	down	Mrpl11	chr19
1426766_at	5.1E-03	491	down	6330403K07Rik	chr11
1430985_at	5.1E-03	493	down	1810027O10Rik	chr11
1417040_a_at	5.1E-03	492	down	Bok	chr1
1437519_x_at	5.1E-03	494	down	Hagh	chr17
1416699_at	5.1E-03	495	down	1110008F13Rik	chr2
1448335_s_at	5.2E-03	496	up	Ccni	chr5
1427153_at	5.2E-03	497	down	Bckdhb	chr9
1452866_at	5.2E-03	498	down	Nars	chr18
1451141_at	5.2E-03	499	down	BC004636	chr2
1437862_at	5.2E-03	500	up	2600011C06Rik	chr12
1422433_s_at	5.2E-03	501	down	ldh1	chr1
1417840_at	5.2E-03	502	down	1500031L02Rik	chr16
1448141_at	5.2E-03	505	down	1110014J01Rik	chr9
1444422_at	5.2E-03	508	up	Pcdh19	chrX
1426646_at	5.2E-03	507	down	9130011J15Rik	chr8
1416143_at	5.2E-03	503	down	Atp5j	chr16
1415911_at	5.2E-03	506	down	Impact	chr18
1415760_s_at	5.2E-03	504	down	Atox1	chr11
1434864_at	5.3E-03	510	down	Nipa1	chr7
1416278_a_at	5.3E-03	509	down	Atp5o	chr12
1443017_at	5.3E-03	512	up	Cpeb2	chr5
1428179_at	5.3E-03	513	down	Ndufv2	chr17
1427822_a_at	5.3E-03	511	up	Copg2as2	
1456341_a_at	5.3E-03	514	up	Klf9	chr19
1451742_a_at	5.3E-03	515	down	Ugp2	chr11
1435602_at	5.3E-03	516	down	Sephs2	chr7
1437283_at	5.4E-03	518	up	Tnpo2	chr8
1421137_a_at	5.4E-03	517	down	Pkib	chr10
1452000_s_at	5.4E-03	521	down	Sars1	chr3
1449012_s_at	5.4E-03	520	down	Fndc4	chr5
1434653_at	5.4E-03	522	up	Ptk2b	chr14
1418311_at	5.4E-03	519	down	Fn3k	chr11
1426245_s_at	5.4E-03	523	up	Mapre2	chr18
1424523_at	5.5E-03	524	down	Elmo1	chr13
1452043_at	5.5E-03	529	down	2310011J03Rik	chr10
1437675_at	5.5E-03	530	up	Slc8a1	chr17
1435738_x_at	5.5E-03	527	down	Serf2	chr2
1428765_at	5.5E-03	526	up	Gtl2	chr12
1428073_a_at	5.5E-03	532	down	Nup88	chr11
1423160_at	5.5E-03	528	up	Spred1	chr2
1422797_at	5.5E-03	531	down	MGI:1932697	chr3
1421875_a_at	5.5E-03	525	down	Mrps23	chr11

1432164_a_at	5.5E-03	533	down	Gcsh	chr8
1442418_at	5.5E-03	535	up	B930096F20Rik	chr19
1434946_at	5.5E-03	534	up	C330021A05Rik	chr12
1420844_at	5.5E-03	536	up	Ubqln2	chrX
1423317_at	5.5E-03	537	down	3110001D03Rik	chr4
1459860_x_at	5.5E-03	539	up	Trim2	
1434393_at	5.5E-03	538	down	Usp34	chr11
1448345_at	5.5E-03	540	down	Tomm34	chr2
1416841_at	5.6E-03	541	down	1110059E24Rik	chr19
1430546_at	5.6E-03	542	down	Cryz11	chr16
1431680_a_at	5.6E-03	543	up	Ptprk	chr10
1435699_at	5.6E-03	544	down	Ppm1l	chr3
1434172_at	5.6E-03	545	up	chr4	
1455228_at	5.6E-03	547	down	chr5	
1435650_at	5.6E-03	548	down	Hapln4	chr8
1423820_at	5.6E-03	546	down	Elof1	chr9
1434887_at	5.6E-03	549	up	Freq	chr2
1416742_at	5.7E-03	551	down	Cfdp1	chr8
1416327_at	5.7E-03	550	down	Ufc1	chr1
1430154_at	5.7E-03	552	down	4930543C13Rik	chr19
1456656_at	5.7E-03	554	up	Lin7a	chr10
1427293_a_at	5.7E-03	553	up	Auts2	chr5
1415820_x_at	5.8E-03	555	down	Nono	chrX
1436349_at	5.8E-03	556	down	2700094K13Rik	chr2
1435392_at	5.8E-03	557	down	Wdr17	chr8
1456759_at	5.8E-03	558	down	6430556C10Rik	chr2
1435026_at	5.8E-03	559	up	Spock2	chr10
1425183_a_at	5.8E-03	560	down	Rpl4	chr9
1416292_at	5.8E-03	561	down	Prdx3	chr19
1451643_a_at	5.8E-03	562	down	Rab4b	chr7
1429515_at	5.8E-03	563	up	Ubr2	chr17
1420354_at	5.8E-03	564	up	Cnnm1	chr19
1429453_a_at	5.8E-03	565	down	Mrpl55	chr11
1450372_a_at	5.8E-03	566	down	Rpl18	chr6
1451018_at	5.8E-03	567	down	Leprotl1	chr8
1438194_at	5.8E-03	568	up	2900019G14Rik	chr2
1447412_at	5.8E-03	569	up	Gm996	chr2
1435152_at	5.9E-03	570	up	Leng8	chr7
1434971_x_at	5.9E-03	571	down		chr1
1455821_x_at	5.9E-03	577	down	C1qbp	chr11
1455377_at	5.9E-03	574	down	4921517B04Rik	chr3
1454655_at	5.9E-03	573	up	Dgkd	chr1
1449921_s_at	5.9E-03	576	up	Cpne6	chr14
1437239_x_at	5.9E-03	575	down	Phc2	chr4
1416921_x_at	5.9E-03	572	down	Aldoa	chr7
1450661_x_at	5.9E-03	578	up	Nfic	chr10
1417236_at	6.0E-03	579	up	Ehd3	chr17
1454843_at	6.0E-03	580	down	Prps2	chrX
1455905_at	6.0E-03	581	up	2610507B11Rik	chr11

1423557_at	6.0E-03	582	down	lfngnr2	chr16
1431411_a_at	6.0E-03	583	down	Rai12	chr11
1436364_x_at	6.0E-03	590	down	Nfix	chr8
1435187_at	6.0E-03	587	down	Tomm20	chr8
1427542_at	6.0E-03	588	up	5330439J01Rik	chr10
1426283_at	6.0E-03	585	up	MGI:2446259	chr9
1419581_at	6.0E-03	589	up	Dlgh4	chr11
1419287_at	6.0E-03	584	down	MGI:1913570	chr8
1416291_at	6.0E-03	586	down	Psmc4	chr7
1424572_a_at	6.0E-03	591	up	H2afy	chr13
1431804_a_at	6.0E-03	592	up	Sp3	chr2
1416567_s_at	6.1E-03	593	down	Atp5e	chr2
1415990_at	6.1E-03	594	down	Vdac2	chr14
1436968_x_at	6.1E-03	595	up	Klhl24	chr16
1434105_at	6.1E-03	597	down	Epm2aip1	chr9
1428382_at	6.1E-03	596	up	Smarcc2	chr10
1450848_at	6.1E-03	598	down	Dap3	chr3
1417075_at	6.2E-03	599	down	2010309E21Rik	chr6
1452927_x_at	6.2E-03	600	down	Tpi1	chr6
1436343_at	6.3E-03	601	up	Chd4	chr6
1450638_at	6.3E-03	603	down	Pdcd5	chr1
1416175_a_at	6.3E-03	602	down	Vdac3	chr14
1444468_at	6.3E-03	604	up	Paqr8	chr1
1449940_a_at	6.4E-03	606	down	Eif2b4	chr5
1421028_a_at	6.4E-03	605	up	Mef2c	chr13
1427908_at	6.4E-03	607	down	Bnip1	chr17
1448609_at	6.4E-03	608	down	Tst	chr15
1448342_at	6.4E-03	610	down	Mapk10	chr5
1431619_a_at	6.4E-03	609	down	Dtnbp1	chr13
1451035_a_at	6.4E-03	611	down	Akr1a4	chr4
1418228_at	6.4E-03	612	down	Hirip5	chr6
1441625_at	6.4E-03	613	up	A930033C01Rik	chr5
1438719_at	6.4E-03	614	up	Al585793	chr18
1460684_at	6.4E-03	615	down	Tm7sf2	chr19
1428428_at	6.4E-03	616	down	Abhd11	chr5
1450068_at	6.5E-03	617	down	Baz1b	chr5
1423597_at	6.5E-03	618	up	Atp8a1	chr5
1418331_at	6.5E-03	619	down	1110031I02Rik	chr11
1452130_at	6.6E-03	620	down	Txndc14	chr2
1437783_x_at	6.6E-03	621	down	Tmem4	chr10
1458870_x_at	6.6E-03	622	up	Phr1	
1440285_at	6.6E-03	623	down	Ppp1r9a	chr6
1427411_s_at	6.6E-03	624	up	Dleu2	chr14
1416850_s_at	6.6E-03	625	down	D10Ert214e	chr10
1436746_at	6.6E-03	626	up	Wnk1	chr6
1423883_at	6.6E-03	627	down	Acsl1	chr8
1437977_at	6.6E-03	628	down	Sgtb	chr13
1427578_a_at	6.6E-03	629	down	ltgb4bp	chr2
1416491_at	6.7E-03	630	up	Numbl	chr7

1415909_at	6.7E-03	631	down	Stip1	chr19
1416486_at	6.8E-03	632	down	Scye1	chr3
1448292_at	6.8E-03	633	down	Uqcr	chr10
1436123_at	6.8E-03	634	up	Bsn	chr9
1435620_at	6.8E-03	635	down	1190002J23Rik	chr1
1438680_at	6.8E-03	636	up	Auts2	chr5
1448753_at	6.9E-03	638	down	Srp9	chr1
1439410_x_at	6.9E-03	637	down	D11Ert333e	chr11
1450906_at	6.9E-03	639	up	Plxnc1	chr10
1453087_at	6.9E-03	640	down	6330403L08Rik	chr5
1428596_at	6.9E-03	641	down	2700008N14Rik	chr11
1448663_s_at	7.0E-03	642	down	Mvd	chr8
1426494_at	7.0E-03	643	down	Rg9mtd3	chr4
1454797_at	7.1E-03	645	down	Tmem55b	chr14
1453207_at	7.1E-03	644	down	LOC554362	chr8
1452044_at	7.1E-03	646	down	Arpc5l	chr2
1434009_at	7.1E-03	647	down	6430596G11Rik	chr7
1434245_a_at	7.2E-03	648	down	Cybasc3	chr19
1433603_at	7.2E-03	649	down	Ndufs6	chr13
1455911_x_at	7.2E-03	655	down	Ndufb11	chr5
1450894_a_at	7.2E-03	656	down	Ap2m1	chr2
1429382_at	7.2E-03	650	down	Nr1i3	chr1
1425845_a_at	7.2E-03	657	up	Shoc2	chr19
1420997_a_at	7.2E-03	651	down	Gpi1	chr7
1416678_at	7.2E-03	653	down	Cops3	chr11
1416185_a_at	7.2E-03	652	down	Adh5	chr3
1415727_at	7.2E-03	654	down	Apoa1bp	chr3
1448868_at	7.2E-03	658	down	Scand1	chr2
1456279_a_at	7.2E-03	660	down	Bcap31	chr10
1452585_at	7.2E-03	659	down	Mrps28	chr3
1438829_at	7.2E-03	663	up	Gm96	chr18
1428499_at	7.2E-03	665	down	2810454L23Rik	chrX
1426360_at	7.2E-03	661	up	Zc3h11a	chr1
1417762_a_at	7.2E-03	664	down	Rpl8	chr15
1416197_at	7.2E-03	662	down	Snrp1c	chr15
1455892_x_at	7.2E-03	666	up		
1449028_at	7.2E-03	670	up	Rhou	chr8
1445534_at	7.2E-03	669	up	Flnb	chr14
1427027_a_at	7.2E-03	668	down	Gtf3a	chr5
1425299_s_at	7.2E-03	667	down	0610038D11Rik	chr19
1435875_at	7.2E-03	672	up	Prkab2	chr3
1434305_at	7.2E-03	671	down	MGC30332	chr7
1419045_at	7.3E-03	674	up	Slc25a23	chr17
1416312_at	7.3E-03	673	down	Rars	chr11
1437852_x_at	7.3E-03	675	down	Cpsf3	chr12
1450866_a_at	7.3E-03	677	down	Mrpl17	chr7
1449234_at	7.3E-03	678	down	Car15	chr16
1418506_a_at	7.3E-03	676	down	Prdx2	chr8
1448263_a_at	7.3E-03	679	down	Cndp2	chr18

1452291_at	7.3E-03	680	down	Centd1	chr5
1422778_at	7.3E-03	681	down	Taf9	chr13
1419924_at	7.3E-03	682	down		chr11
1428540_at	7.4E-03	684	up	3321401G04Rik	chr6
1415783_at	7.4E-03	683	down	Vps35	chr8
1415766_at	7.4E-03	685	down	4930564D15Rik	chr3
1457366_at	7.4E-03	688	up	Cdc40	chr10
1439421_x_at	7.4E-03	687	down	chr1	
1417126_a_at	7.4E-03	686	down	Rpl22l1	chr3
1453421_at	7.5E-03	690	down	Srr	chr11
1437774_at	7.5E-03	689	up	1700020I14Rik	chr2
1428076_s_at	7.5E-03	691	down	Ndufb4	chr16
1435659_a_at	7.5E-03	692	down	Tpi1	chr6
1442026_at	7.6E-03	693	up		chr9
1427510_at	7.7E-03	694	up	Gnai1	chr5
1442867_at	7.7E-03	696	up	2410080H04Rik	chr9
1423692_at	7.7E-03	698	down	Ndufa8	chr2
1422556_at	7.7E-03	697	up	Gna13	chr11
1416859_at	7.7E-03	695	down	Fkbp3	chr12
1435500_at	7.7E-03	701	down	Rab26	chr17
1429106_at	7.7E-03	700	down	4921509J17Rik	chr3
1426894_s_at	7.7E-03	699	down	C230093N12Rik	chr2
1434065_at	7.7E-03	702	down	Cwf19l1	chr19
1456444_at	7.7E-03	703	up	Fbxo41	chr6
1457361_at	7.8E-03	704	up	C630007C17Rik	chr2
1452662_a_at	7.8E-03	705	down	Eif2s1	chr12
1415859_at	7.8E-03	706	up	Eif3s8	chr7
1418814_s_at	7.8E-03	707	down	Ndufa12	chr10
1417028_a_at	7.8E-03	708	up	Trim2	chr3
1455283_x_at	7.8E-03	709	down	Ndufs8	chr19
1420628_at	7.8E-03	710	down	Pura	chr18
1460304_a_at	7.8E-03	711	up	Ubf	chr11
1452479_at	7.8E-03	712	up	Copg2as2	
1458685_at	7.8E-03	713	up	Garnl1	chr12
1437288_at	7.9E-03	714	up	Impad1	chr4
1417050_at	7.9E-03	716	down	C1qtnf4	chr2
1416119_at	7.9E-03	715	down	Txn1	chr1
1452742_at	7.9E-03	717	up	2310001H13Rik	chr9
1429244_at	7.9E-03	718	down	2610524H06Rik	
1426340_at	7.9E-03	719	up	Slc1a3	chr15
1419493_a_at	8.0E-03	720	down	Tpd52	chr3
1460554_s_at	8.0E-03	722	down	Glg1	chr8
1452189_at	8.0E-03	721	down	9430077D24Rik	chr9
1427437_at	8.0E-03	724	up	chr9	
1417058_a_at	8.0E-03	723	down	Krtcap2	chr3
1416636_at	8.0E-03	725	down	Rheb	chr5
1448406_at	8.0E-03	727	up	Cri1	chr2
1433616_a_at	8.0E-03	726	down	2310028O11Rik	chr4
1436902_x_at	8.1E-03	728	down	Tmsb10	chr7

1428554_a_at	8.2E-03	729	down	1810035L17Rik	chr12
1437001_at	8.2E-03	730	up	Gsk3b	chr16
1435067_at	8.2E-03	732	down	B230208H17Rik	chr2
1424091_at	8.2E-03	731	down	AI449175	chr8
1416367_at	8.2E-03	733	down	1110001J03Rik	chr6
1424751_at	8.3E-03	734	down	Abt1	chr13
1451080_at	8.4E-03	735	down	Usp1	chr4
1425531_at	8.4E-03	736	down	Znhit1	chr5
1448112_at	8.4E-03	737	down	Cox7c	chr11
1435866_s_at	8.6E-03	738	down	Hist3h2a	chr11
1423966_at	8.6E-03	740	up	Cd99l2	chrX
1423958_a_at	8.6E-03	739	down	2900001O04Rik	chr15
1418171_at	8.6E-03	741	down	Tceal8	chrX
1445502_at	8.7E-03	742	up	chr8	
1438735_at	8.7E-03	743	up	Hbxap	chr7
1459984_at	8.7E-03	745	up	Mia3	chrUn
1416807_at	8.7E-03	744	down	Rpl36a	chrX
1457744_at	8.7E-03	753	up	Ddx46	chr13
1457248_x_at	8.7E-03	748	down	Hsd17b7	chr1
1450662_at	8.7E-03	746	down	Tesk1	chr4
1450070_s_at	8.7E-03	750	down	Pak1	chr7
1437118_at	8.7E-03	752	up	Usp7	chr16
1434882_at	8.7E-03	749	up	Mtdh	chr15
1429582_at	8.7E-03	755	up	Btbd14a	chr2
1424350_s_at	8.7E-03	756	up	Lpgat1	chr1
1424313_a_at	8.7E-03	758	down	Ndufs7	chr10
1421751_a_at	8.7E-03	747	down	Psmc14	chr2
1419509_a_at	8.7E-03	754	down	Nagk	chr6
1417472_at	8.7E-03	751	up	Myh9	chr15
1415791_at	8.7E-03	757	down	Rnf34	chr5
1438344_at	8.8E-03	760	up	4833424O15Rik	chr3
1421504_at	8.8E-03	759	up	Sp4	chr12
1452825_at	8.8E-03	763	down	5330410G16Rik	chr8
1448203_at	8.8E-03	761	down	Atp5l	chr9
1417046_at	8.8E-03	762	down	Tusc4	chr9
1420416_at	8.8E-03	764	down	Sema3a	chr5
1449980_a_at	8.8E-03	767	down	Gabrd	chr4
1443225_at	8.8E-03	766	up	Acvr1c	chr2
1428362_at	8.8E-03	765	down	E130105L11Rik	chr7
1428465_at	8.9E-03	768	down	5033425B17Rik	chr7
1438771_at	8.9E-03	769	up	Brd1	chr15
1435337_at	9.0E-03	770	down	Zfp537	chr7
1425573_a_at	9.0E-03	772	up	Ddef1	chr15
1423240_at	9.0E-03	771	up		chr2
1422580_at	9.0E-03	774	down	Myl4	chr11
1417879_at	9.0E-03	773	down	Nenf	chr1
1424365_at	9.1E-03	775	down	1810037I17Rik	chrX
1449187_at	9.2E-03	777	down	Pdgfra	chr5
1428584_a_at	9.2E-03	778	down	Haghl	chr17

1426432_a_at	9.2E-03	776	up	Slc4a4	chr5
1448726_at	9.2E-03	779	down	Snapc2	chr8
1455662_x_at	9.2E-03	780	down	Rps17	chr7
1451988_s_at	9.2E-03	782	down	Chmp4b	chr2
1451540_at	9.2E-03	781	down	Mpi1	chr9
1448542_at	9.3E-03	783	down	Bccip	chr7
1448524_s_at	9.3E-03	784	down	Ssr4	chrX
1460637_s_at	9.3E-03	785	down	Pfdn5	chr15
1449648_s_at	9.3E-03	786	down	Rpo1-1	chr17
1446565_at	9.3E-03	787	up	Man1b	
1449435_at	9.4E-03	788	down	B4galt3	chr1
1443694_at	9.4E-03	789	down	Rgs20	chr1
1439767_at	9.4E-03	791	up	Dlgap2	chr8
1429579_at	9.4E-03	792	down	6330407118Rik	chr9
1427909_at	9.4E-03	794	down	2410015M20Rik	chr17
1426862_at	9.4E-03	793	up	9130023F12Rik	chr11
1426341_at	9.4E-03	797	up	Slc1a3	chr15
1424207_at	9.4E-03	795	up	Smarca5	chr4
1416894_at	9.4E-03	796	down	1500019G21Rik	chr7
1415860_at	9.4E-03	790	down	Kpna2	chr4
1436113_a_at	9.5E-03	798	down	St13	chr15
1434702_at	9.5E-03	799	down	2600009E05Rik	chr2
1452333_at	9.5E-03	801	up	Smarca2	chr19
1450818_a_at	9.5E-03	802	down	Ndufa7	chr17
1428515_at	9.5E-03	800	down	2410012H22Rik	chr11
1440443_at	9.5E-03	803	up	E030016H06Rik	chr2
1455081_at	9.5E-03	804	down	Txn14b	chr8
1448625_at	9.5E-03	806	down	Golga2	chr2
1447995_x_at	9.5E-03	805	down	1700026B20Rik	chr12
1452629_at	9.5E-03	807	up	Safb2	chr17
1441645_s_at	9.5E-03	808	down	lpo9	chr1
1436949_a_at	9.5E-03	809	down	Tceb2	chr17
1435171_at	9.6E-03	810	down	2810416G20Rik	chr3
1440729_at	9.6E-03	812	up	Eps15	chr4
1416595_at	9.6E-03	813	down	Mrps22	chr9
1453187_at	9.7E-03	815	down	Ociad2	chr5
1421141_a_at	9.7E-03	814	up	Foxp1	chr6
1423035_s_at	9.7E-03	817	down	Txn15	chr11
1422467_at	9.7E-03	816	down	Ppt1	chr4
1427254_at	9.7E-03	818	up	Zfp445	chr9
1450147_at	9.7E-03	827	up	Nptxr	chr15
1447404_at	9.7E-03	819	down	G630064H08Rik	chr18
1426480_at	9.7E-03	823	down	Sbds	chr5
1426468_at	9.7E-03	821	down	0610037L13Rik	chr4
1424364_a_at	9.7E-03	822	down	1110020P15Rik	chr11
1424163_at	9.7E-03	826	down	0610039K22Rik	chr11
1423109_s_at	9.7E-03	825	down	Slc25a20	chr9
1422264_s_at	9.7E-03	824	up	Klf9	chr19
1418444_a_at	9.7E-03	820	down	MGI:1891827	chr7

1428589_at	9.7E-03	829	down	Mrpl41	chr2
1423833_a_at	9.7E-03	828	down	Brp44	chr1
1439578_at	9.8E-03	830	up	Lsm11	chr11
1452659_at	9.9E-03	831	down	Dek	chr13
1418185_at	9.9E-03	832	down	4733401H18Rik	chr9
1417083_at	1.0E-02	833	down	Sec61b	chr4
1456041_at	1.0E-02	834	down	Snx16	chr3

HPC

1452434_s_at	5.2E-11	0	down	Dgcr6	chr16
1428190_at	3.1E-10	1	down	Slc25a1	chr16
1449183_at	3.9E-10	2	down	Comt	chr16
1418087_at	7.2E-09	3	down	Ufd1l	chr16
1448900_at	7.2E-09	4	down	D16H22S680E	chr16
1448849_at	2.3E-08	5	down	Mrpl40	chr16
1452357_at	2.3E-08	6	down	Gp1bb	chr16
1422547_at	4.4E-08	7	down	Ranbp1	chr16
1421810_at	6.9E-08	8	down	Dgcr2	chr16
1428753_a_at	1.3E-07	9	down	Dgcr6	chr16
1421809_at	3.2E-07	10	down	Dgcr2	chr16
1432367_a_at	1.5E-06	11	down	Ufd1l	chr16
1448114_a_at	1.7E-06	12	down	Htf9c	chr16
1436468_at	2.9E-06	13	down	Zdhhc8	chr16
1460033_at	3.2E-06	14	up	C030002C11Rik	chr1
1417629_at	3.8E-06	15	down	Prodh	chr16
1419732_at	7.2E-06	16	down	Rtn4r	chr16
1448115_at	8.5E-06	17	down	Htf9c	chr16
1418701_at	1.0E-05	18	down	Comt	chr16
1435179_at	1.4E-05	19	up	C130071C03Rik	chr13
1436241_s_at	1.9E-05	20	down	Hira	chr16
1435089_at	3.5E-05	21	up	2010111I01Rik	chr13
1441312_at	9.0E-05	22	up		chr19
1422977_at	9.4E-05	23	down	Gp1bb	chr16
1455326_at	1.1E-04	24	up	4932416N17Rik	chr16
1440357_at	1.1E-04	25	up		chr15
1424038_a_at	1.2E-04	26	up	2310044H10Rik	chr7
1435439_at	1.3E-04	27	down	Dgcr8	chr16
1457030_at	1.4E-04	28	up	Mirg	chr12
1450467_at	1.5E-04	29	up	Bsn	chr9
1416822_at	1.8E-04	30	down	Es2el	chr16
1450855_at	2.7E-04	31	down	Arvcf	chr16
1455311_at	3.7E-04	32	down	Dgcr8	chr16
1427410_at	5.2E-04	33	up	Dleu2	chr14
1449888_at	5.2E-04	34	up	Epas1	chr17
1422733_at	5.3E-04	35	up	Fjx1	chr2
1423125_at	6.6E-04	36	up	Dcamkl1	chr3
1433450_at	1.1E-03	37	up	Cdk5r1	chr11
1420506_a_at	1.2E-03	38	up	Stxbp1	chr2
1452742_at	1.2E-03	39	up	2310001H13Rik	chr9

1441391_at	1.2E-03	40	down	Gnb1l	chr9
1423061_at	1.3E-03	41	down	Arvcf	chr16
1457675_at	1.3E-03	42	down	2510002D24Rik	chr16
1438196_at	1.5E-03	43	up	Gpd1l	chr9
1436796_at	1.8E-03	44	down	1110061A14Rik	chr18
1460650_at	1.9E-03	45	up	Atp6v0a1	chr11
1425691_at	2.1E-03	46	up	B3gat1	chr9
1442072_at	2.2E-03	47	up	C230081A13Rik	chr9
1421890_at	2.3E-03	48	up	St3gal2	chr8
1428562_at	2.5E-03	49	up	2210403K04Rik	chr11
1419049_at	2.6E-03	50	up	Pcnx	chr12
1420833_at	3.2E-03	51	up	Vamp2	chr11
1423915_at	3.3E-03	52	up	Olfml2b	chr1
1425461_at	3.5E-03	53	up	Fbxw11	chr11
1416821_at	3.7E-03	54	down	Es2el	chr16
1418151_at	3.7E-03	55	up	Mtmt4	chr11
1441782_at	4.1E-03	56	up	Aak1	chr6
1431254_at	4.4E-03	57	up	Kbtbd11	chr8
1416132_at	4.5E-03	58	up	C920006C10Rik	chr15
1449931_at	4.6E-03	59	up	Cpeb4	chr11
1425690_at	4.6E-03	61	up	B3gat1	chr9
1450913_at	4.6E-03	60	up	B4galt6	chr18
1450166_at	4.7E-03	62	up	Ids	chrX
1428986_at	4.9E-03	63	up	Slc17a7	chr7
1460164_at	4.9E-03	64	up	Spin	chr13
1428739_at	4.9E-03	66	down	2310040A07Rik	chr4
1460617_s_at	4.9E-03	65	up	Rab6b	chr9
1421123_at	5.2E-03	67	up	Cdk5r1	chr11
1437118_at	5.4E-03	68	up	Usp7	chr16
1431214_at	5.5E-03	70	up	1300007C21Rik	
1415804_at	5.5E-03	69	up	Cx3cl1	chr8
1422223_at	6.3E-03	71	up	Grin2b	chr6
1454706_at	6.3E-03	72	up	Uvrag	chr7
1449097_at	6.4E-03	73	down	Txnrd2	chr16
1455836_at	6.4E-03	74	up	Papola	chr12
1450955_s_at	6.4E-03	75	up	Sort1	chr3
1452490_a_at	6.5E-03	76	up	Ap2a2	chr7
1420816_at	6.6E-03	81	up	Ywhag	chr5
1434244_x_at	6.6E-03	77	down	Htf9c	chr16
1451992_at	6.6E-03	80	up	Adrbk1	chr19
1434751_at	6.6E-03	79	up	Ids	chrX
1455000_at	6.6E-03	78	up	Gpr68	chr12
1452747_at	6.9E-03	82	up	Atp13a2	chr4
1421580_at	7.1E-03	83	up	Cntnap1	chr11
1422966_a_at	7.7E-03	84	up	Tfrc	chr16
1438255_at	8.0E-03	85	down	Ches1	chr12
1449961_at	8.2E-03	86	up	Rph3a	chr5
1456283_at	8.3E-03	87	up	Neto1	chr18
1417839_at	8.4E-03	88	down	Cldn5	chr16

1421200_at	8.7E-03	89	up	Dlgh2	chr7
1424476_at	9.6E-03	90	up	Camkk2	chr5
1427254_at	9.8E-03	91	up	Zfp445	chr9
1452226_at	9.8E-03	92	up	Rcc2	chr4
1450849_at	9.8E-03	93	up	Hnrpu	chr1

Supplementary Table 2. Probe sets located outside *Df(16)A* and included in the common PFC/HPC gene list (FDR *P*-value < 0.01)

Probe Set ID	Gene Name	Chr	PFC			HPC			miRNA(s) within the gene
			FDR <i>P</i> -value	Fold Change	Direction	FDR <i>P</i> -value	Fold Change	Direction	
1460033_at	<i>C030002C11Rik</i>	chr1	2.24E-07	2.05	up	3.22E-06	1.76	up	mir-29b-2, 29c
1440357_at		chr15	2.24E-07	2.33	up	1.06E-04	1.93	up	mir-let-7b,let-7c-2
1428562_at	<i>2210403K04Rik</i>	chr11	3.56E-07	1.43	up	2.47E-03	1.39	up	mir-22
1457030_at	<i>Mirg</i>	chr12	3.63E-07	1.66	up	1.45E-04	1.80	up	mirna clusters. mir-134
1435179_at	<i>C130071C03Rik</i>	chr13	2.40E-06	1.47	up	1.42E-05	1.50	up	mir-9-2
1435089_at	<i>2010111I01Rik</i>	chr13	1.41E-05	1.87	up	3.53E-05	1.67	up	mir-23b, 27b,24-1
1424038_a_at	<i>2310044H10Rik</i>	chr7	1.70E-05	1.45	up	1.17E-04	1.38	up	
1455326_at	<i>4932416N17Rik</i>	chr16	1.70E-05	1.65	up	1.06E-04	2.09	up	
1433450_at	<i>Cdk5r1</i>	chr11	5.79E-04	1.18	up	1.11E-03	1.18	up	
1436796_at	<i>1110061A14Rik</i>	chr18	1.04E-03	1.29	down	1.80E-03	1.35	down	
1422733_at	<i>Fjx1</i>	chr2	2.70E-03	1.59	up	5.32E-04	1.75	up	
1425691_at	<i>B3gat1</i>	chr9	2.86E-03	1.36	up	2.09E-03	1.44	up	
1425690_at	<i>B3gat1</i>	chr9	3.87E-03	1.48	up	4.64E-03	1.39	up	
1450467_at	<i>Bsn</i>	chr9	4.46E-03	1.51	up	1.46E-04	1.58	up	
1428986_at	<i>Slc17a7</i>	chr7	4.93E-03	1.24	up	4.87E-03	1.30	up	
1452742_at	<i>Trak1</i>	chr9	7.85E-03	1.44	up	1.18E-03	1.54	up	
1437118_at	<i>Usp7</i>	chr16	8.74E-03	2.79	up	5.35E-03	2.59	up	
1427254_at	<i>Zfp445</i>	chr9	9.66E-03	1.25	up	9.80E-03	1.32	up	

Supplementary Table 3. Probe Set List that overlap a miRBase miRNA-containing primary transcript

Probe Set ID	PFC			HPC			Gene Symbol
	FDR <i>P</i> - value	Fold Change	Direction	FDR <i>P</i> - value	Fold Change	Direction	
1416568_a_at	4.74E-03	1.54	up	9.32E-02	1.39	up	<i>Acin1</i>
1423160_at	5.46E-03	1.29	up	3.96E-01	1.08	up	<i>Spred1</i>
1423162_s_at	8.96E-04	1.93	up	8.70E-02	1.55	up	<i>Spred1</i>
1427410_at	1.07E-02	1.52	up	5.22E-04	1.82	up	<i>Dleu2</i>
1427411_s_at	6.60E-03	1.54	up	6.48E-02	1.38	up	<i>Dleu2</i>
1427437_at	8.00E-03	1.54	up	3.18E-01	1.11	up	<i>2610203C20Rik</i>
1428562_at	3.56E-07	1.43	up	2.47E-03	1.39	up	<i>2210403K04Rik</i>
1428764_at	2.12E-04	1.45	up	3.16E-01	1.39	up	<i>Gtl2</i>
1428765_at	5.46E-03	1.11	up	2.65E-01	1.14	up	<i>Gtl2</i>
1434730_at	2.07E-07	1.38	up	2.34E-01	1.13	up	<i>A1854517</i>
1435089_at	1.41E-05	1.87	up	3.53E-05	1.67	up	<i>2010111I01Rik</i>
1435179_at	2.40E-06	1.47	up	1.42E-05	1.50	up	<i>C130071C03Rik</i>
1436746_at	6.60E-03	1.57	up	3.96E-01	1.20	up	<i>Wnk1</i>
1439305_at	7.32E-05	1.95	up	4.77E-02	1.40	up	
1440097_at	3.39E-03	1.27	up	2.30E-01	1.24	up	<i>Mirg</i>
1440357_at	2.24E-07	2.33	up	1.06E-04	1.93	up	
1445502_at	8.67E-03	1.52	up	8.65E-02	1.30	up	
1457030_at	3.63E-07	1.66	up	1.45E-04	1.80	up	<i>Mirg</i>
1457336_at	4.71E-03	1.72	up	3.33E-01	1.45	up	<i>R3hdm1</i>
1460033_at	2.24E-07	2.05	up	3.22E-06	1.76	up	<i>C030002C11Rik</i>
1460695_a_at	6.06E-04	1.43	up	2.22E-01	1.17	up	<i>2010111I01Rik</i>

Supplementary Table 4: miRNAs down-regulated in PFC and HPC of *Df(16)A*^{+/-} mice

miRNA (mmu-miR)	Locus	FDR P-value	Fold Change	Chr	Chr_start	Chr_end	Strand	Note
PFC								
185	185	3.6E-08	0.42	16	18240964	18241028	-	
134	134	2.2E-04	0.62	12	110181946	110182016	+	
665	665	2.2E-04	0.64	12	110034121	110034214	+	
674	674	2.2E-04	0.65	2	116876568	116876667	+	
532	532	3.3E-04	0.66	X	6405361	6405456	-	
673	673	6.6E-04	0.55	12	110019797	110019887	+	
674*	674*	1.3E-03	0.68	2	116876568	116876667	+	
224	224	1.4E-03	0.27	X	68513751	68513832	-	
491	491	1.4E-03	0.60	4	87593271	87593356	+	
744	744	1.4E-03	0.77	11	65550928	65551027	-	
377	377	1.4E-03	0.45	12	110188317	110188384	+	
93	93	1.5E-03	0.83	5	138395311	138395398	-	
383	383	1.7E-03	0.75	8	39720650	39720719	-	
212	212	1.8E-03	0.77	11	74989583	74989673	+	
22	22	2.0E-03	0.80	11	75279911	75280005	+	
378	378	3.0E-03	0.70	18	61523204	61523269	-	
422b	422b	3.1E-03	0.59	18	61523204	61523269	-	renamed mir-378
425	425	3.5E-03	0.66	9	108426880	108426964	+	
700	700	3.5E-03	0.60	4	134688631	134688709	-	
299	299	4.0E-03	0.54	12	110158445	110158507	+	
324-5p	324-5p	4.1E-03	0.76	11	69828238	69828326	+	
342	342	4.1E-03	0.80	12	109106427	109106525	+	
345	345	4.1E-03	0.71	12	109284780	109284875	+	
467*	467*	4.1E-03	0.79	2	10394199	10394271	+	low complexity repeat
540	540	4.1E-03	0.41	12	110033887	110033953	+	
708	708	4.1E-03	0.58	7	96124616	96124724	+	
770-3p	770-3p	4.1E-03	0.73	12	110011499	110011592	+	
106b	106b	4.8E-03	0.80	5	138395525	138395606	-	
541	541	4.8E-03	0.77	12	110190216	110190305	+	
99b	99b	4.8E-03	0.81	17	17534806	17534875	+	
140*	140*	6.1E-03	0.59	8	110440373	110440442	+	
194	194-1	6.1E-03	0.74	1	187014107	187014173	+	two locations in mouse genome
194	194-2			19	6264643	6264728	+	
325	325	6.1E-03	0.66	X	101581801	101581898	-	
494	494	6.1E-03	0.55	12	110163125	110163209	+	
362	362	7.5E-03	0.53	X	6398941	6399005	-	
107	107	7.9E-03	0.81	19	34886684	34886770	-	
154	154	8.6E-03	0.83	12	110186240	110186305	+	
324-3p	324-3p	9.9E-03	0.74	11	69828238	69828326	+	
350	350	9.9E-03	0.78	1	178609000	178609098	-	
338	338	1.3E-02	0.62	11	119830855	119830952	-	
676*	676*	1.4E-02	0.76	X	96583816	96583904	+	
329	329	1.6E-02	0.80	12	110161288	110161384	+	
409	409	1.7E-02	0.78	12	110190965	110191043	+	
323	323	1.7E-02	0.77	12	110160315	110160400	+	
103	103-1	1.7E-02	0.82	11	35625819	35625904	+	two locations in mouse genome
103	103-2			2	130979493	130979578	+	
505	505	1.9E-02	0.52	X	56741073	56741162	-	
133a	133a-1	2.1E-02	0.74	18	10782907	10782974	-	two locations in mouse genome
133a	133a-2			2	180327787	180327890	+	
								low complexity repeat mmu-mir-669a-1 at chr2:10394706-10394802
669a	669a	2.1E-02	0.67	2	10394706	10394802	-	
151	151	2.2E-02	0.78	15	73082071	73082138	-	

125b	125b-1	2.6E-02	0.82	9	41332995	41333071	+	two locations in mouse genome
125b	125b-2			16	77528865	77528935	+	
455-3p	455-3p	2.8E-02	0.76	4	62743212	62743293		
18	18	3.0E-02	0.70	14	113925688	113925783	+	
291b-5p	291b	3.6E-02	0.68		--	--		unknown location
100	100	4.6E-02	0.82	9	41282494	41282573	+	
412	412	4.6E-02	0.72	12	110191096	110191175	+	
192	192	4.7E-02	0.75	19	6264844	6264932	+	
337	337	4.7E-02	0.67	12	110033596	110033692	+	
122a	122a	4.8E-02	0.25	18	65374230	65374295	+	
186	186	4.8E-02	0.51	3	157479572	157479642	+	
25	25	4.8E-02	0.81	5	138395109	138395192	-	

HPC

185	185	6.5E-12	0.41	16	18240964	18241028	-	renamed mir-37 8
422b	422b	4.8E-06	0.54	18	61523204	61523269	-	
674	674	1.0E-05	0.75	2	116876568	116876667	+	
673	673	1.3E-05	0.64	12	110019797	110019887	+	
674*	674*	1.4E-05	0.69	2	116876568	116876667	+	
409	409	3.2E-05	0.78	12	110190965	110191043	+	
151	151	4.5E-05	0.78	15	73082071	73082138	-	
540	540	1.0E-04	0.53	12	110824290	110824356	+	
212	212	1.2E-04	0.73	11	74989583	74989673	+	
532	532	2.7E-04	0.61	X	6405361	6405456	-	
140*	140*	4.2E-04	0.67	8	110440373	110440442	+	
494	494	5.1E-04	0.58	12	110163125	110163209	+	
491	491	1.4E-03	0.69	4	87593271	87593356	+	
224	224	1.4E-03	0.29	X	68513751	68513832	-	
325	325	1.8E-03	0.73	X	101581801	101581898	-	
134	134	2.5E-03	0.57	12	110181946	110182016	+	
153	153	2.7E-03	0.71	12	117692826	117692894	+	two locations in mouse genome
153								
93	93	2.9E-03	0.73	5	138395311	138395398	-	
200a	200a	3.4E-03	0.54	4	155429005	155429094	-	
29c	29c	3.5E-03	0.72	1	196738271	196738358	+	
323	323	3.5E-03	0.81	12	110160315	110160400	+	
379	379	4.0E-03	0.78	12	110947270	110947335	+	
106b	106b	4.0E-03	0.73	5	138395525	138395606	-	
18	18	4.4E-03	0.64	14	113925688	113925783	+	
362	362	4.9E-03	0.67	X	6398941	6399005	-	
194	194-1	5.5E-03	0.74	1	187014107	187014173	+	two locations in mouse genome
194	194-2			19	6264643	6264728	+	
383	383	6.9E-03	0.75	8	39720650	39720719	-	
29a	29a	7.2E-03	0.74	6	30992823	30992910	-	
669a	669a	1.1E-02	0.75	2	10394706	10394802	+	low complexity repeat, mmu-mir-669a-1 at chr2:10394706-10394802
708	708	1.2E-02	0.67	7	96124616	96124724	+	

Supplementary Table 5. Primers and probes used in qRT-PCR

Name	Sequence
<i>Dgcr8</i> -exon6-8-L	AATGGGAAGTCTGAGTTTGC
<i>Dgcr8</i> -exon6-8-P	ACATGCAGCGTGTCTCAAGGTC
<i>Dgcr8</i> -exon6-8-R-2	AGTTCCAGATCCGTAAGTCACAC
<i>Dgcr8</i> -exon8-9-L	GGAGAAGCCTAAAGACAGTGAA
<i>Dgcr8</i> -exon8-9-P	TAACCACATCAGTATTGAGGATTCA
<i>Dgcr8</i> -exon8-9-R	GGAGACAACAGCCCAGCCT
<i>Dgcr8</i> -F	CCACGACCATCCTCAGACATTG
<i>Dgcr8</i> -R	ATGAAAATCTCCCCTCCCACAGCC
Gene trap-R	ACGCCATACAGTCCTCTTCAC
<i>Mirg</i> -L	GACATTCCACTGGGGACATC
<i>Mirg</i> -P	CCTGAGCCCTGACCTGAAGCC
<i>Mirg</i> -R	GGAGGCCACAAAGTCAGGTA
Pri-134_L1	CTTGGTGAGGCAGCTGTG
Pri-134_P1	TGGCACCAACATCTCTCCGGA
Pri-134_R1	AACCAGTCACACACCCTGAA
Pri-154_L1	AGGTTATCCGTGTTGCCTTC
Pri-154_P1	CCAAATCCCGCCTTGGAGGA
Pri-154_R1	CTGGAAAGACGCTAACACCA
Pri-186-L1	TCAGACTGTGGAGTCTTGTTG
Pri-186-P1	6CAGTCCTACAGTTCCAGAGGGCC[3BQ1]
Pri-186-R1	AAGGAGAATTCTTTGGAAAGTTG
Pri-26a-1-F	GCAGAACTCCAGAGAGAAGGAAGGTA
Pri-26a-1-P	AAGCTGGAGGACCGAGGC
Pri-26a-1-R	GACCTGCACAGCCTATCCTGGAT
Pri-29b_L1	GGTTTCACATGGTGGCTTAG
Pri-29b_P1	TGTAGTCTACCCTCTGCTGTGCTGCA
Pri-29b_R1	CTCGAAGGAGAGAGCCAGTT
Pri-29C_L1	CCAGTCGGTCCATCTCTTACA
Pri-29C_P1	CAGGCTGACCGATTTCTCCTGG
Pri-29C_R1	GTGCTCTTCCCCCTACATCAT
Pri-30d-F	CAGCATCCTCAGCTCCAATCCTT
Pri-30d-P	CCAGATTGTCCAAAAGAT
Pri-30d-R	TGTAAGCCACAGCCAAGCTTTCA
Pri-330-L1	TTGTTGCTGTTGCCTAGGAG
Pri-330-P1	6CCGGTCTTCCAGGATCGCGT[3BQ1]
Pri-330-R1	CTTTGCTCGTTGGATCTTGA
Pri-382-F	TGGAAACCATAGCCCTTGGAGAA
Pri-382-P	CCCTTTGTCTGTCTTGTCTC
Pri-382-R	AAGCGAATCCACCACGAACAAC
Pri-410-F	CAGGACAGCTTCAGGTGGTGATT
Pri-410-P	CAGCTCCAGGGTTGC
Pri-410-R	CGTCATTAATAAAGCGAACTCATCACA
Pri-488-L1	ACTTCAGCAGGAAGAATGCC
Pri-488-P1	6TCCCAGCTGGAGCTTCCTCCA[3BQ1]
Pri-488-R1	CAGCCTTTCAAACAACATGG
Pri-671-L1	AGCAGAGGGCTGCTTCTACA
Pri-671-P1	6AGGAGGAAGCCCTGGAGGGG[3BQ1]

Pri-671-R1	CTGAGAACCGGAGGAAAACA
Pri-9_L1	ATCTGGAGTTCAGCCAGAGG
Pri-9_P1	TCGCTTCCCTCACAAGGCTGC
Pri-9_R1	CGGTGACCTTGAAGGAGTTT
Pri-92-1-F	AAAAGTCTGTAGAGAAGTAAGGGAAAATCAAA
Pri-92-1-P	CCCTTTCTACACAGGTTGGG
Pri-92-1-R	CCGGGACAAGTGCAATACCATAC
Pri-98-F	GGTAGGGATTTTAGGCCCCAGTAA
Pri-98-P	AGATAACTATACAACTTACTACTTTCCTTG
Pri-98-R	AATGGAGTCAATACTGCCAAGACTTAATG
<i>Drosha</i> -F	GGATAGGCTGTGGGAAAGGA
<i>Drosha</i> -R	CTTCTTGATGTCTTCAGCCTCC
<i>Drosha</i> -P	AGAAGCGGTTTCATTGAGCGGAAA
<i>Dicer1</i> -F	TGCTCGAGATGGAACCAGA
<i>Dicer1</i> -R	TCAGCTGTTAGGAACCTGAGGC
<i>Dicer1</i> -P	TACAGGATCGCCAAGTCTGCTGC

SUPPLEMENTARY NOTE

Production of mice with a deficiency at the orthologous 22q11.2 locus. By using a chromosomal engineering approach¹, we generated a mouse model carrying a 1.3-Mb deficiency on chromosome 16 syntenic to the human 22q11.2 region ranging from the *Dgcr2* gene to the *Hira* gene and encompassing 27 genes (*Df(16)A*^{+/-}, **Suppl. Fig. 1A**). Targeting constructs for the 5' and 3' ends of the deficiency were introduced into *HPRT*-deficient AB2.2 ES cells through homologous recombination (**Suppl. Fig. 1B**). Exposure to Cre recombinase *in vitro*, followed by selection in hypoxanthine-aminopterin-thymidine (HAT) media, led to the generation of ES cells with the expected deficiency. Chimeric mice were generated and germline transmission of the deficiency was achieved and confirmed by Southern blot and PCR analysis (**Suppl. Fig. 1C**). Fluorescent in situ hybridization (FISH) analysis of mice following two or three generations of backcrossing demonstrated that the deficiency was present and stable through at least 3 backcross generations (**Suppl. Fig. 1D**). Mice harboring the deficiency appeared normal by gross observation, although, consistent with previous results² we obtained fewer *Df(16)A*^{+/-} adult mice (37.3%, $n = 300$) than the 50% transmission rate expected from heterozygote (HET) X wild-type (WT) crosses. A fraction of HET mice were found previously to die at birth or shortly thereafter, apparently from a number of cardiovascular abnormalities, which have been characterized at E18.5 and E13.5^{2,3}. Milder forms of cardiac abnormalities were found to persist in 18% of surviving adult mice². *Df(16)A*^{+/-} mice do not show any gross anatomical brain abnormalities, but show deficits in synaptic connectivity in the HPC, which can be partially accounted for by deficiency in the *Zdhhc8*⁴ gene (Mukai et al., submitted).

Pavlovian fear conditioning. Our results are consistent with the study of Paylor et al.⁵ that also showed deficits in contextual learning in a mouse strain carrying a smaller deficiency. Since the Paylor et al. study did not identify a deficit in the cued conditioning test, we re-examined this task and reproduced our findings in a second cohort of male mice (see **Suppl. Fig. 2A**).

Comparison with previous expression profiling studies at this locus. There are 2 independent studies^{6,7} that have used expression profiling in mouse models of this locus. We provide below a comparison between these studies and the present. The first study, Sivagnanasundaram et al.⁶, used a mouse strain (*Dfl*^{+/-}) that carries a smaller chromosomal deficiency (*Dfl*), which is not found in humans and does not include five genes that are deleted in the mouse strain used in the present study. They also used Affymetric GeneChip (MOE430A), which includes approximately 22K probe sets for only known genes, while the present study used MOE430 2.0, which includes 45K probe sets (all genes on both MOE430A and MOE430B). MOE430B includes approximately 23K ESTs and therefore our analysis has higher chance to identify transcripts that are not related to known genes (including many of the ones shown to contain miRNA genes). They also used only 3 mutant and 3 WT mice, and therefore their study lacks power as compared to our study, which used 10 pairs of animals. These authors employed a Per chip positive control and per gene median normalization method. By contrast, we used the well-established GC-RMA method for data normalization, which controls for both within and between chip variation. In addition, they used an arbitrary cutoff *P*-value to control for multiple testing, whereas we employed the widely used False Discovery Rate

(FDR) Method. Notably, Sivagnanasundaram et al.⁶ failed to detect the expected reduction in all of the genes included within the chromosomal deficiency. By contrast, in our study, all the genes within the 22q11 deficiency were found to be reduced by ~50%, consistent with the Jurata et al.⁷ and Meechan et al.⁸ studies. Despite all these differences we attempted to compare our results with those of Sivagnanasundaram et al.⁶ To facilitate comparisons we used nominal *P*-values because Sivagnanasundaram et al.⁶ do not report FDR-corrected *P*-values. When we consider the 27 differentially expressed probe sets reported by Sivagnanasundaram et al.⁶ we find that approximately 1/3 of these probe sets show nominally significant *P*-values and similar trend of fold-change in our dataset (data not shown). However, all these probe sets are removed after we apply FDR correction.

The second study, Jurata et al.⁷, also used mice carrying the smaller Df1 deficiency, as well as a different expression platform (Agilent Mouse Oligo Array 22K, containing about 20,371 genes: 16,359 known genes, 4,509 genes with no Refseq names). They focused on one HPC structure (dentate gyrus), which they isolated via laser-capture microdissection and therefore had to conduct an RNA amplification step. Although they use a comparable to ours set of animal pairs ($n = 12$), they conduct a LOWESS normalization for each chip, but no correction between chips. They also do not apply any multiple testing correction for their significant *P*-values. As a result, they report a high false positive rate in their results. For these reasons, direct comparison of our results and those of Jurata et al.⁷ is difficult. Nevertheless, it is worth noting that one of the most (nominally) significant expression differences they report is for EST (AI854517), which is part of EST AK032343, which contains mir-9-3. Consistent with our findings, the

Jurata et al.⁷ study reported an up-regulation of 1.2-fold for this miRNA-containing transcript.

PFC/HPC shared gene list. Inspection of the PFC/HPC shared gene list (**Suppl. Table 2**) revealed several known genes, such as *B3gat1* (previously associated with a schizophrenia-like psychosis through molecular analysis of a balanced translocation⁹), *Bsn* and *Slc17a7/vGlut1* (both important components of glutamatergic synapses), as well as *Cdk5r* (the regulatory subunit of cyclin-dependent kinase 5, the major kinase that opposes the phosphatase activity of calcineurin, which has been previously implicated in schizophrenia¹⁰). The PFC/HPC shared gene list also included the *Mirg* gene, a non-coding RNA gene, which is highly expressed in the adult brain and contains the largest miRNA cluster in the mouse genome^{11,12}. Probe sets from the *Mirg* gene indicated transcript up-regulation, a finding confirmed with quantitative RT-PCR (qRT-PCR) using primers from the 3' end of the gene (see **Fig. 3A, B**, main manuscript). The contribution of these genes to the 22q11-associated psychiatric and cognitive deficits is the focus of ongoing investigation (BX, JAG, MK, unpublished data).

Production of *Dgcr8*-deficient mice (see **Fig. 4**, main manuscript). We generated *Dgcr8*-deficient mice using an ES cell line (XH157 ES, BayGenomics) carrying a β -geo gene trap inserted into intron 8 of the *Dgcr8* gene (**Fig. 4A, B**). A transcriptional fusion, expected to be generated as a result of splicing between the splice donor site at *Dgcr8* exon 8 and the splice acceptor site located at the gene trap (expected size ~7.5-kb), was detected in Northern blots using mRNA extracted from total brain of HET mice (**Fig.**

4C). As expected, by using qRT-PCR we showed that the full-length *Dgcr8* mRNA levels are reduced by approximately half in *Dgcr8*-deficient mice ($P = 0.0001$) (**Fig. 4D**). At the protein level, we can also readily detect by Western blots, using total brain protein extracts, a chimeric protein produced as a result of the translational fusion between the N-terminal part of *Dgcr8* and the β -geo moiety (expected size ~220-kD) and the reduced WT 120-kD product (**Fig. 4E**). As a result of the translational fusion, one of the two functional double-stranded RNA binding domains of *Dgcr8* is truncated, whereas the second one is completely eliminated in this chimeric protein which is, therefore, predicted to have severely impaired activity. Consistent with this prediction, homozygous mice die before birth (unpublished data).

Normal hearing of *Dgcr8*-deficient mice. To control against confounding effects of impaired hearing, we examined the response of *Dgcr8*^{+/-} mice to startle stimuli, ranging from background (70 dB) to 118 dB. At each of the lowest intensities used in the PPI protocol (74 – 86 dB) there were no significant differences in startle between genotypes ($P > 0.05$, see **Suppl. Fig. 2B**). Also, within-genotype comparisons to the background level (70 dB) revealed that *Dgcr8*^{+/-} mice first show significant ($P < 0.05$) startle response over background at 90 dB, whereas WT mice first show significant response at 94 dB.

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SUPPLEMENTARY METHODS

Gene targeting and generation of *Df(16)A*^{+/-} mice. Two mouse genomic libraries were used: the 5' *HPRT* library and the 3' *HPRT* library. The 5' *HPRT* vector backbone contains a *LoxP* site, exons 1 and 2 of the *HPRT* minigene, a coat color marker (tyrosinase minigene), and a neomycin resistance selection marker. The 3' *HPRT* vector backbone contains a *LoxP* site, exons 3 to 9 of the *HPRT* minigene, a coat color marker (K14 agouti transgene), and a puromycin resistance selection marker. The 5' *HPRT* library was screened for *Dgcr2* and the 3' *HPRT* library was screened for *Hira*. Both 5' and 3' constructs were obtained, linearized within the genomic inserts (using *NheI* for the 5' construct and *NdeI* for the 3' construct), and electroporated into ES cells. After introduction of the 5' vector (25 µg of DNA was used), the clones were selected in 180 µg/ml of G418 for 8 – 10 days. The 3' vector was then introduced (25 µg of DNA was used) and the clones were selected in 3 µg/ml of Puromycin for 8 – 10 days. To confirm the proper insertion of the 5' and 3' targeting constructs, we used a combination of Southern blot and PCR-based analyses. The ES cells used were the AB2.2 ES cell line, which is derived from *HPRT*-deficient 129S5/SvEvBrd mice¹.

In order to achieve recombination between the *loxP* sites, we used 2 approaches. In the first approach, we electroporated a Cre recombinase-expressing construct (pOG231)² into doubly-targeted clones at the ES cell stage. Selection of the re-arranged chromosomes was possible in HAT media, since a functional *HPRT* minigene was produced when the two halves of the *HPRT* minigene were fused during the rearrangement. Doubly targeted clones were electroporated with the pOG231 Cre plasmid. Clones were selected in HAT (0.1 mM sodium hypoxanthine, 0.2 µM

aminopterin, and 0.016 mM thymidine) for 8 – 10 days and released in HT (0.1 mM sodium hypoxanthine and 0.016 mM thymidine) for 48 h.

Following Cre-mediated recombination, ES clones were amplified and injected into C57BL/6J blastocysts. Resulting chimeric males were bred to C57BL/6J females in order to obtain F1 mice. Southern blot analysis on a *KpnI* digest of tail DNA was used to confirm the presence of the deficiency. A 24.8-kb band indicating an expected change in the location of *KpnI* sites when the deletion was achieved, and an expected 7.4-kb WT band were detected. Once these mouse lines were confirmed by Southern blot analysis, maintenance was performed by PCR genotyping. Primers were selected such that an 829-bp band could be detected when the 5' and 3' insertions were directly abutted upon recombination. Primer 1 is within the 5' construct, inside human *HPRT* exon 2: 5'-ATTCCCCATGGACTAATTATGGACAGG-3'. Primer 2 is inside the 3' construct, within human *HPRT* intron 2: 5'-GGTATCTCCATAAGACAGAATGCTATGC-3'. The PCR cycling conditions we used were: 94°C for 3 min; 35 cycles of 94°C for 30 s, 60°C for 1 min, and 72°C for 1 min; 72°C for 10 min. A second set of primers: 5'-CTAGGCCACAGAATTGAAAGATCT-3' and 5'-GTAGGTGGAAATTCTAGCATCATCC-3' was included in these assays in order to detect a 324-bp *IL-2* internal control band.

In the second approach, we generated mice using ES clones containing non-recombined 5' and 3' *loxP* sites. For these lines, probes external to the 5' *Dgcr2* insert and external to the 3' *Hira* insert were used to verify the 5' and 3' insertions. In each case, mouse genomic DNA was prepared from tail clips of HET mice and digested with *SpeI*. Southern blot analysis detected a 20.6-kb band, demonstrating the proper positioning of the 5' insertion, in addition to a 15.6-kb WT band. For the 3' insert,

probing of *SpeI* cut DNA revealed a 14.5-kb band indicating the proper positioning of the 3' construct, in addition to an expected 17.7-kb WT band. Once these mouse lines were confirmed by Southern blot analysis, maintenance was performed by PCR genotyping. PCR primers were used to detect the puromycin resistance gene. 5'-ATGACCGAGTACAAGCCCAC-3' and 5'-GCGTGAGGAAGAGTTCTTGC-3' primers led to the generation of a 166-bp PCR product. The PCR cycling conditions we used were: 94°C for 3 min; 35 cycles of 94°C for 30 s, 65°C for 30 s, and 72°C for 90 s; then 72°C for 10 min. These mice were bred with mice expressing Cre recombinase in their germline: *HPRT-Cre* (stock # 004302), *Prm-Cre* (stock # 003328) and *Zp3-Cre* (stock # 003651), all obtained from The Jackson Laboratory, Bar Harbor, ME. Offspring that were positive by PCR for both the puromycin resistance gene (see PCR conditions above) and *Cre recombinase* (using primers 5'-GCGGTCTGGCAGTAAAACTATC-3' and 5'-GTGAAACAGCATTGCTGTCACCTT-3', and cycling conditions 94°C for 3 min; 35 cycles of 94°C for 30 s, 51°C for 1 min, and 72°C for 1 min; then 72°C for 10 min) were bred with C57BL/6J WT mice. The resulting offspring from these crosses were screened for the presence of the deficiency (*Df(16)A*) by using the primers and PCR conditions described above. We found that only the crosses using the *HPRT-Cre* mice led to the production of deletion mice. For the experimental studies described in this paper, the mice used were those in which the deletion was generated by exposure to Cre recombinase at the ES cell stage. Behavioral assays were performed on mutant mice and their WT littermates following a three-generation backcross of the mutations into the C57BL/6J background.

Fluorescent *In Situ* hybridization (FISH). FISH was performed at the Molecular Cytogenetics Core Facility at the Memorial Sloan-Kettering Cancer Center in New York. Mouse chromosome 16 BAC clones from within the deletion region [BACs RP23-47O21 (obtained from BACPAC Resources) and RP23-55L18 (from Invitrogen)] and outside the deletion region [BACs RP23-290E4 and RP23-356A24, both purchased from Invitrogen] were differentially labeled and used as fluorescent probes. Metaphase chromosome spreads were prepared from splenocyte cultures obtained from 4 mice heterozygous for the deletion.

Behavioral analysis: *Open field activity assay.* Mouse activity was monitored in a clear illuminated acrylic chamber equipped with infrared sensors to automatically record horizontal and vertical activity (Colbourn Instruments). Each mouse was initially placed in the center of the chamber and its activity was recorded and collected in 1-min bins. The floors of the open field were cleaned with 70% ethanol between mice. Overall, 26 *Df(16)A^{+/-}* mice and 22 WT controls of either sex were tested in the open field assays. For *Dgcr8^{+/-}* testing, 9 male *Dgcr8^{+/-}* mice and 9 male WT littermate controls were used. *Light/dark transition testing.* The open field activity box (Colbourn Instruments) was fitted with an acrylic insert that divided the box into a dark right half and a light left half, with a small doorway through which mice could pass. A lamp with a 60-W light bulb was positioned above the open field, thus providing extra illumination. Group-housed mice were removed from their home cages and placed into the dark side. Their activity was automatically recorded for 15 min. Twenty males (11 *Df(16)A^{+/-}* mice, 9 WT littermate controls) and 15 females (8 *Df(16)A^{+/-}* mice, 7 WT littermate controls) were tested.

PPI analysis. Acoustic startle and PPI of acoustic startle responses were recorded using two startle monitor chambers (Hamilton-Kinder). Trial types, trial type presentation, and background noise levels were performed according to the protocols described previously⁴ with some modifications. For the *Df(16)A^{+/-}* mice, both male (21 *Df(16)A^{+/-}* and 19 WT littermate controls) and female mice were tested (10 *Df(16)A^{+/-}* and 10 WT littermate controls). For the *Dgcr8^{+/-}* mice, 10 male and 10 WT male littermate controls were used. Percent PPI was calculated as 100-[(startle response of acoustic startle from acoustic prepulse and startle stimulus trials/startle response alone trials) x 100]. A separate startle response curve session for the *Dgcr8^{+/-}* mice included recordings made every 4 dBs above background (70 dB), up to 114 dB. *Cognitive tasks.* Both tasks were performed as described previously^{3,4}. In both the Pavlovian fear conditioning and the spatial working memory test, 10 males (*Df(16)A^{+/-}* or WT controls) and 10 females (*Df(16)A^{+/-}* or WT controls), as well as 15 males (*Dgcr8^{+/-}* or WT controls) were tested.

Statistical analysis. Statistical analysis was performed in STATVIEW (SAS Institute, Cary, NC). Data was analyzed by ANOVA or repeated-measures ANOVAs.

RNA isolation for expression profiling. We dissected a total of 20 PFC and 20 HPC from 10 *Df(16)A^{+/-}* mutants and 10 WT control mice. All mice were male littermates 8 weeks of age. Tissues were processed using standard protocols recommended by Affymetrix. RNA quality was assessed with Bioanalyzer (Agilent Technologies, Palo Alto, CA). For hybridization, cRNA was fragmented and exposed to Affymetrix Mouse genome 430 2.0 array set chips (which include 45,000 probe sets from > 34,000 well characterized mouse genes). Sequence clusters were created and refined from UniGene

and the Whitehead Institute Center for Genome Research databases. After hybridization, microarrays were washed and scanned (Agilent).

Gene class testing and pathway analysis. We used two independent statistical approaches, ErmineJ⁵ and gene-set-enrichment analysis (GSEA)⁶, which compare the number of genes in a class that show significant changes in expression with the number expected under a particular null hypothesis. After correction for multiple testing there was significant convergence between the two approaches, thus providing additional confidence in the findings. Normalized and log transformed raw data and FDR *P*-values of all probe sets were imported into gene class scoring analysis software ErmineJ and GSEA. Gene classes were defined using Gene Ontology (GO) terms, nested functional categories that summarize the known cellular components, molecular functions and biological processes. The GO database includes all known genes grouped into tree-like structure of the cellular components, biological processes or molecular functions. The significant GO terms branches were combined using Amigo (<http://www.godatabase.org/cgi-bin/amigo/go.cgi>) and visualized using Graphviz software (<http://www.graphviz.org/>). The significance levels were set to 0.05 in both ErmineJ and GSEA analyses.

Pathway analysis was performed using the PathwayAssist software (Version 3.0, Ariadne Genomic) as an interface to map our significant gene list (FDR *P*-value < 0.05 and fold change ≥ 1.2) onto ResNet, a comprehensive database of signaling pathways identified via literature mining. Specifically, the PathwayAssist software was used to further investigate if some of the significantly changed genes share the same biological

pathway or interact with each other as indicated by literature references. Significantly changed genes were imported into PathwayAssist and the ResNet Core database was used for the annotation. At FDR P -value < 0.05 and fold change ≥ 1.2 , there were 375 differentially expressed probe sets in HPC. Of them, 132 probes matched known genes in the ResNet database.

Quantitative RT-PCR of the miRNA pri-forms. Total RNA from PFC and HPC was extracted from 8-wk old male mice using the same protocol as for the microarray study. We used 6 *Df(16)A*^{+/-} mice and 6 WT littermate controls, as well as 6 *Dgcr8*^{+/-} mice and 6 WT littermate controls. We used 5 μ g of RNA per sample for reverse transcription reactions. RNA was first subjected to DNAase digestion using the DNA-free kit (Ambion) and reverse-transcribed using Superscript II reverse transcriptase (Invitrogen) according to the company manuals. We pooled 3 μ l of the resulting cDNA from each sample as the template for the qRT-PCR standard curve. The rest of the cDNA was diluted 1:15 before preparing the qRT-PCR reaction. qRT-PCR was conducted using the ABI Taqman method. All PCR primers and Taqman probes were designed at two web sites (<https://www.genscript.com/ssl-bin/app/primer> and http://frodo.wi.mit.edu/cgi-bin/primer3/primer3_www.cgi) and purchased from Sigma Genosys (Sigma-Aldrich). All target gene probes were 5' FAM and 3' BHQTM-1 Dual labeled. Mouse *glyceraldehyde-3-phosphate dehydrogenase (GAPDH)* mRNA was used as the endogenous control. The *GAPDH* gene probe was 5' JOETM and 3' BHQTM-1 dual labeled. For each sample, a duplex PCR reaction was set-up containing a target gene primer probe set and a *GAPDH* primer probe set. We conducted 5 replicate PCR reactions for each sample. The reactions were incubated in a 96-well plate at 95°C for 10 min, followed by 45 cycles of 95°C for

15 sec and 60°C for 1 min on a 7700 Sequence Detection System (Applied Biosystems). The relative levels of gene expression were determined according to the standard curve methods described in the ABI company manual (Applied Biosystems). The expression value of the target gene in each well was first normalized by the expression value of the *GAPDH* gene in the same well. The median of 5 repeated reactions was used to represent the relative quantity of the target gene. A student's *t*-test was conducted to identify the significant differences between the mutant mice and their corresponding WT littermate controls.

Quantitative RT-PCR of the miRNA mature forms. Total RNA samples of PFC were extracted from 8-wk old male mice using the mirVana™ miRNA Isolation Kit (Ambion) according to the manufacturer's protocol. We used 6 *Df(16)A^{+/-}* mice and 6 WT littermate controls, as well as 6 *Dgcrδ^{+/-}* mice and 6 WT littermate controls. Purified total RNA was eluted in 100 µl of elution buffer. We first treated 5 µg total RNA with DNA-free kit (Ambion). Then, 100 ng treated RNA was reverse transcribed and qRT-PCR was performed using the TaqMan® MicroRNA PCR kit and Mouse TaqMan® MicroRNA Assays according to the company's protocol (Applied Biosystems). A *GAPDH* gene-specific RT primer was included in the RT reaction and a duplex reaction that included target miRNA primer and probe set, as well as *GAPDH* primer and probe set was used in the subsequent qPCR reactions. The reactions were incubated in a 96-well plate at 95°C for 10 min, followed by 45 cycles of 95°C for 15 sec and 60°C for 1 min on a 7700 Sequence Detection System (Applied Biosystems). All reactions were repeated 5 times. The relative quantity was determined in the same way described in the previous section.

Northern blot analysis. The probe for *Dgcr8* was amplified using primers from exon 8 (5'-TGAAGGACAATGAGGAACGAG-3') and exon 9 (5'-CTCGAGTAATACGACTCACTATAGGAGGCTCACTTGGATTCTCACA-3') designed based on the *Dgcr8* full length cDNA sequence (GeneBank; NM_033324). DIG-labeled RNA probe was then synthesized from the PCR product using the DIG Northern Starter Kit (Roche). Total RNA was extracted from mouse whole brain using Trizol reagent (Invitrogen) and mRNA was isolated using the PolyATtract® mRNA Isolation System III (Promega). 1 µg of mRNA per sample was resolved on a 1.2% denatured agarose gel and transferred to a Hybond-N+ nylon membrane (GE Healthcare). The blot was pre-hybridized in Easyhyb (Roche) at 68°C for 1 h. Hybridization was then performed at 68°C overnight. The wash and immunological detection steps were carried out according to the instructions of the DIG Northern Starter Kit (Roche).

Western blot analysis. Total brains were homogenized in lysis buffer containing 1% Triton X-100, 0.2 mM EDTA, 100 mM KCl and 20 mM Tris pH 8.0 and Proteinase inhibitor cocktail (Roche). Homogenates were centrifuged at 12,000 x g at 4°C for 30 min. The supernatant was saved and the protein concentration in each sample was determined. An aliquot of the supernatant equivalent to 15 – 20 µg protein was resolved on 8% SDS-PAGE and then transferred onto a nitrocellulose membrane (Schleicher and Schuell Bioscience, Inc). The membrane was first blocked by 5% nonfat dry milk in PBS buffer containing 0.5% Tween-20 for 1 h at room temperature. The membrane was then washed three times with the same buffer and treated with 1:400 diluted *Dgcr8* primary antibody (ProteinTech Group Inc). The membrane was washed again with the same buffer three times, treated with 1:5000 dilution of horseradish peroxidase conjugated

secondary antibody for 1 h at room temperature and then washed thoroughly. The washed membrane was incubated with HRP substrate (Western Lightning Chemiluminescence Reagent, PerkinElmer Life Sciences) for 1 min, exposed to Kodak X-Omat AR X-ray film (Eastman Kodak) and developed. The membrane was then stripped and re-probed with α -actin antibody (Santa Cruz) as a loading control, using the same procedure described above.

Nissl Staining. Mice were perfused with 4% PFA and fixed overnight in 4% PFA at 4°C. Brains were then incubated in 30% sucrose overnight at 4°C and sectioned using a cryostat. Sections were collected, mounted on slides and dried overnight. Sections were then defatted in xylene for 30 min at room temperature twice, re-hydrated in 100% EtOH (3 min) followed by 95% EtOH (3 min) and stained in cresyl violet for 3 – 5 min. After rinsing in distilled water for 2 min, sections were then soaked in 95% EtOH for 5 min, dehydrated in 100% EtOH for 5 min, cleared in xylene for 5 min and then mounted on slides with Permount (Fisher Scientific). Images were taken with bright field microscope.

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