

Supplemental Information

Supplemental Figures

Figure S1

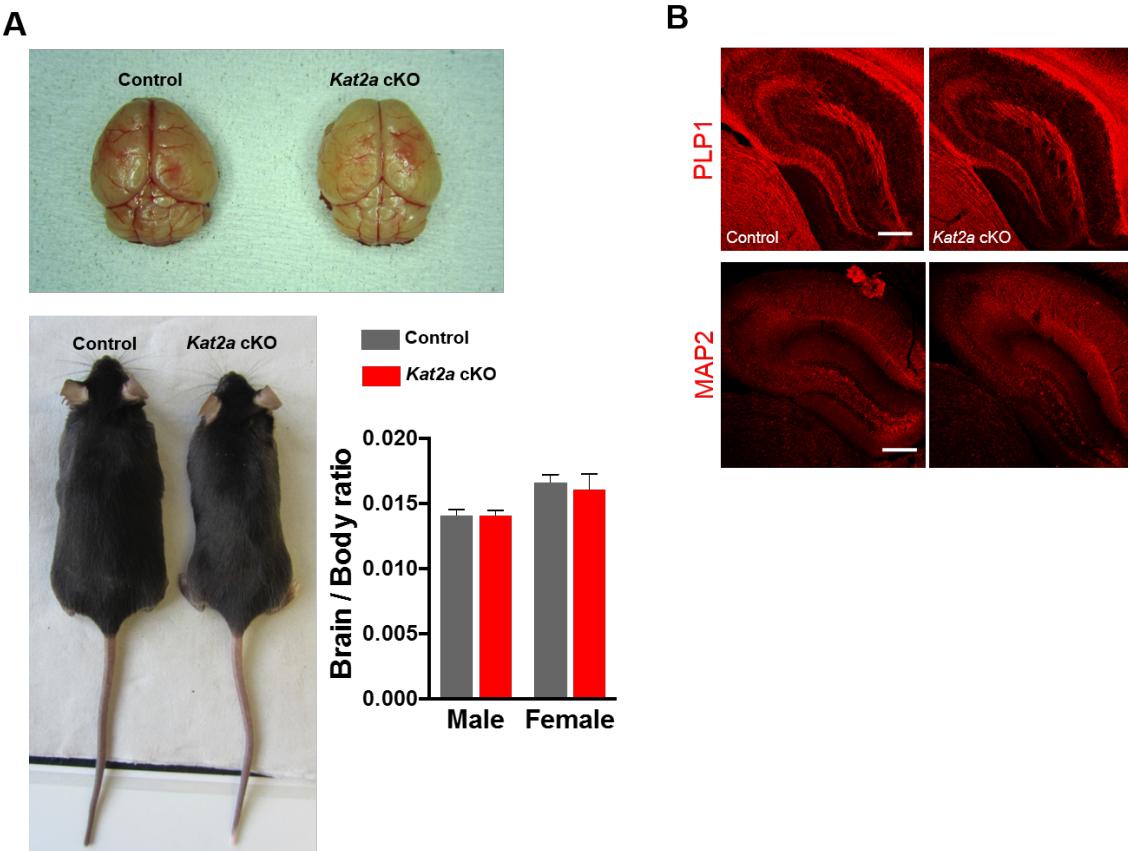


Figure S1. Loss of KAT2A does not alter gross brain morphology. A. Upper panel: Representative images of non-fixed brains (olfactory bulbs removed) of male control and *Kat2a* cKO mice. Lower left panel: Representative images of male mice from both groups. Lower right panel: Quantification of brain weight over body weight ratio. There was no difference between control (n=21) and *Kat2a* cKO (n=16) animals. In both groups, males (n=14 vs. 12) showed lower ratios compared to females (n=7 vs. 4). **B.** Representative images showing hippocampal immunoreactivity for oligodendrocyte marker PLP1 and post-synaptic marker MAP2 in control and *Kat2a* cKO mice (n=4/group) Scale bar:150 μ m. Error bar represent S.E.M.

Figure S2

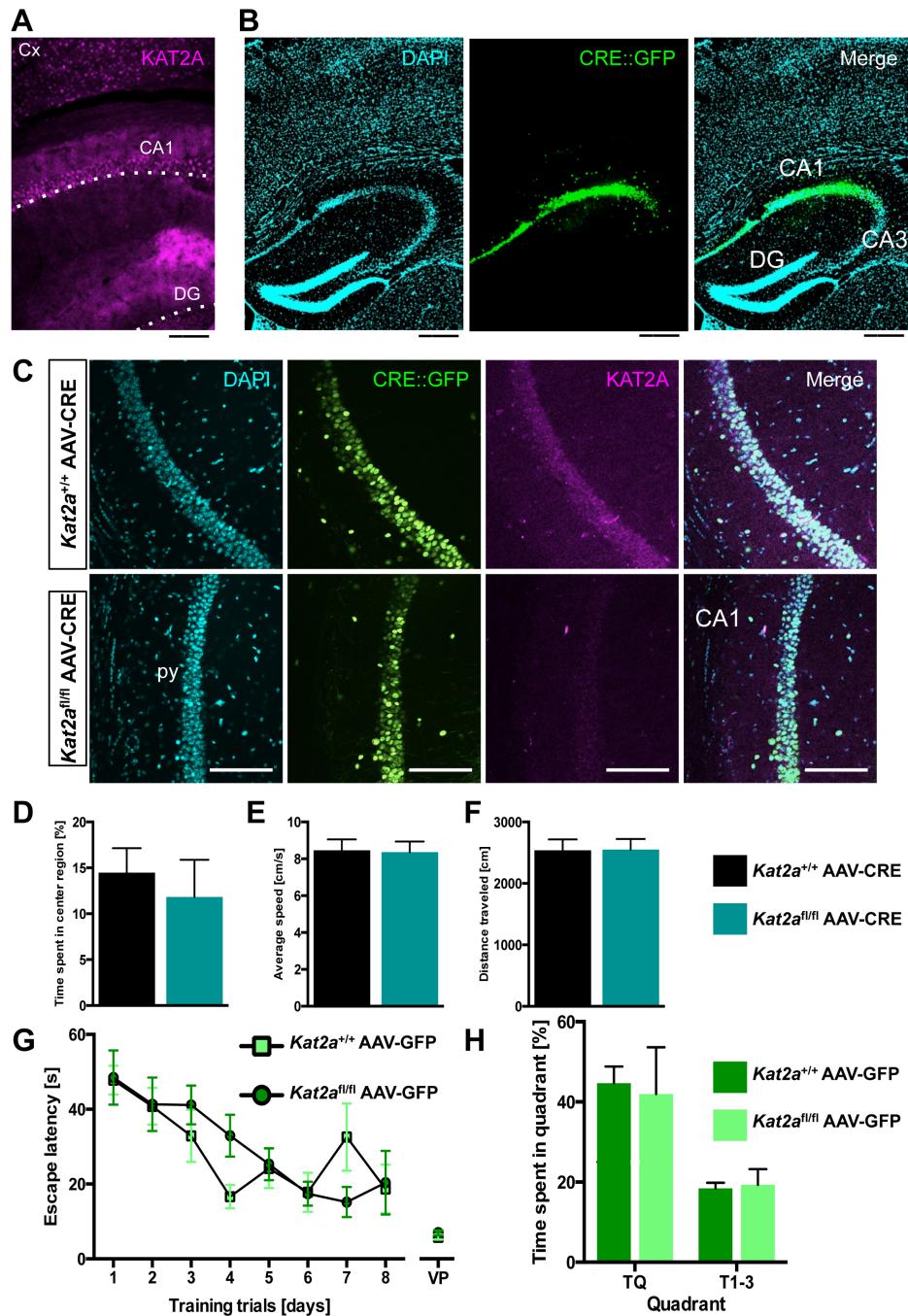


Fig. S2. KAT2A in the CA1 region does not affect basal anxiety, motor function and short-term plasticity.

A. Representative immunostaining showing KAT2A expression in the cortex (Cx) as well as in CA1 and DG. Scale bar 150 μ m. **B.** Representative micrographs showing expression of Cre::GFP fusion protein after AAV injection. Detectable expression was limited to CA1. Scale bar: 250 μ m. **C.** Representative immunostainings showing the reduction of KAT2A in the hippocampal CA1 pyramidal (py) layer of *Kat2a^{fl/fl}* AAV-CRE mice compared to wild type controls (*Kat2a^{+/+}* AAV-CRE). Scale bar: 250 μ m, **D-F.** Open field test for *Kat2a^{fl/fl}* AAV-CRE mice compared to controls. No differences were found for the tested parameters ‘Time spent in center region’ (**D**), ‘Average speed’ (**E**), and ‘Distance traveled’ (**F**). **G-H.** AAV-GFP was injected in the CA1 of *Kat2a^{fl/fl}* and wild type controls (*Kat2a^{+/+}*) and mice were subjected to the Morris water maze (n=5/group). There was neither a difference during the acquisition phase (**G**), nor during probe test (**H**). VP: visual platform.

Figure S3

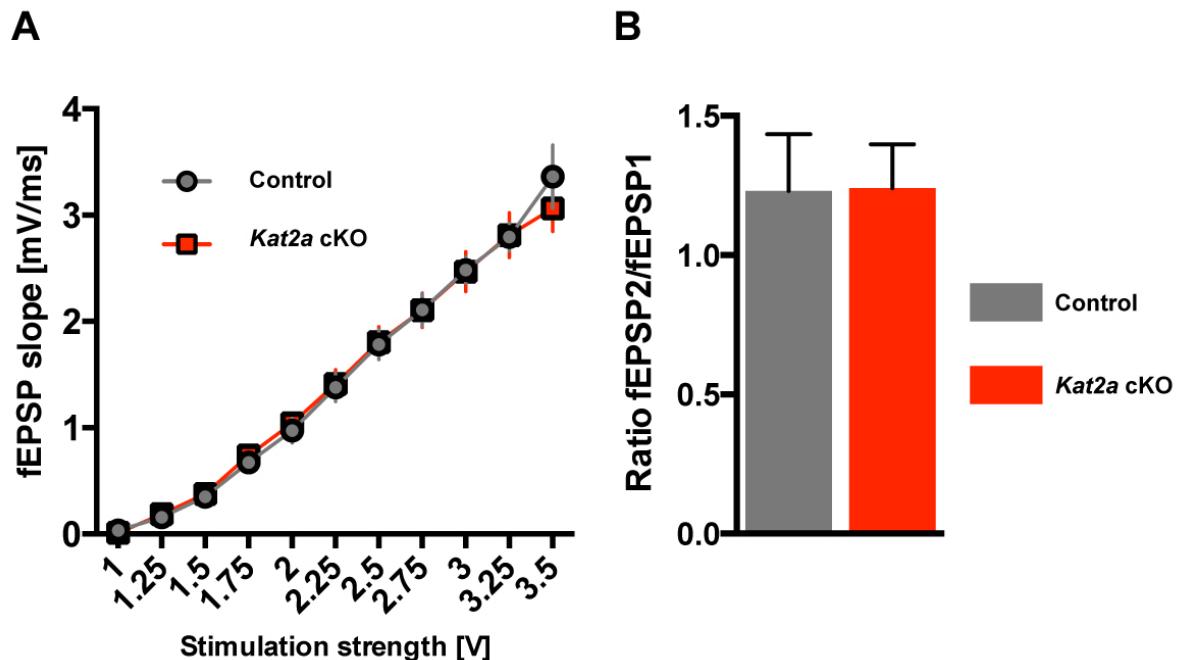


Fig. S3. CA1 specific plasticity controlled by KAT2A.

A. To establish input-output relationships for hippocampal CA3-CA1 synapses the slopes of fEPSPs were plotted against the stimulation protocol. Basal synaptic transmission was normal in *Kat2a* cKO and control mice (n= 5/group). B. Paired pulse facilitation tested in *Kat2a* cKO and control mice (n=5/group). The ratios of second over first fEPSP slopes were plotted. There was no significant difference among groups. Error bar represent S.E.M.

Figure S4

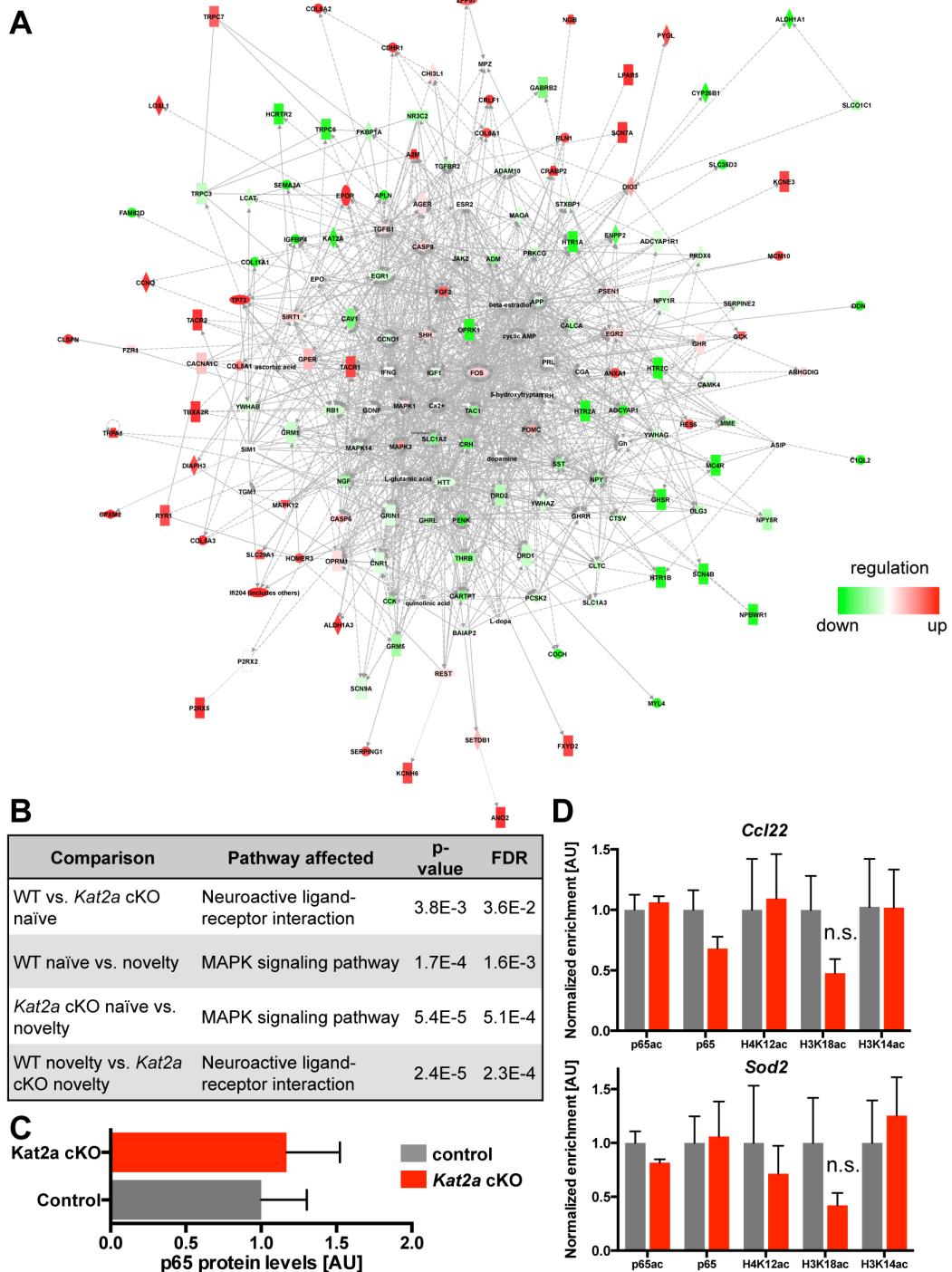


Fig. S4. CA1 specific gene-expression network controlled by KAT2A.

A. Network analysis of differentially regulated genes between control and *Kat2a* cKO mice in the CA1 region. For network analysis we used all genes differentially expresses amongst *Kat2a* cKO and control mice under naïve or novelty induced conditions. **B.** Major pathways affected by KAT2A. Please note that the major pathway affected by novelty was MAPK signaling, which was independent of KAT2A function. **C.** Relative protein levels as determined by western blot for p65 (n=4/group). There was no difference between groups. **D.** ChIP at promoters known NF-κB-target genes (*Ccl22* and *Sod2*), which were not regulated in *Kat2a* cKO mice. Primers were designed to amplify the predicted NF-κB binding site. There was no significant difference between groups.

Figure S5

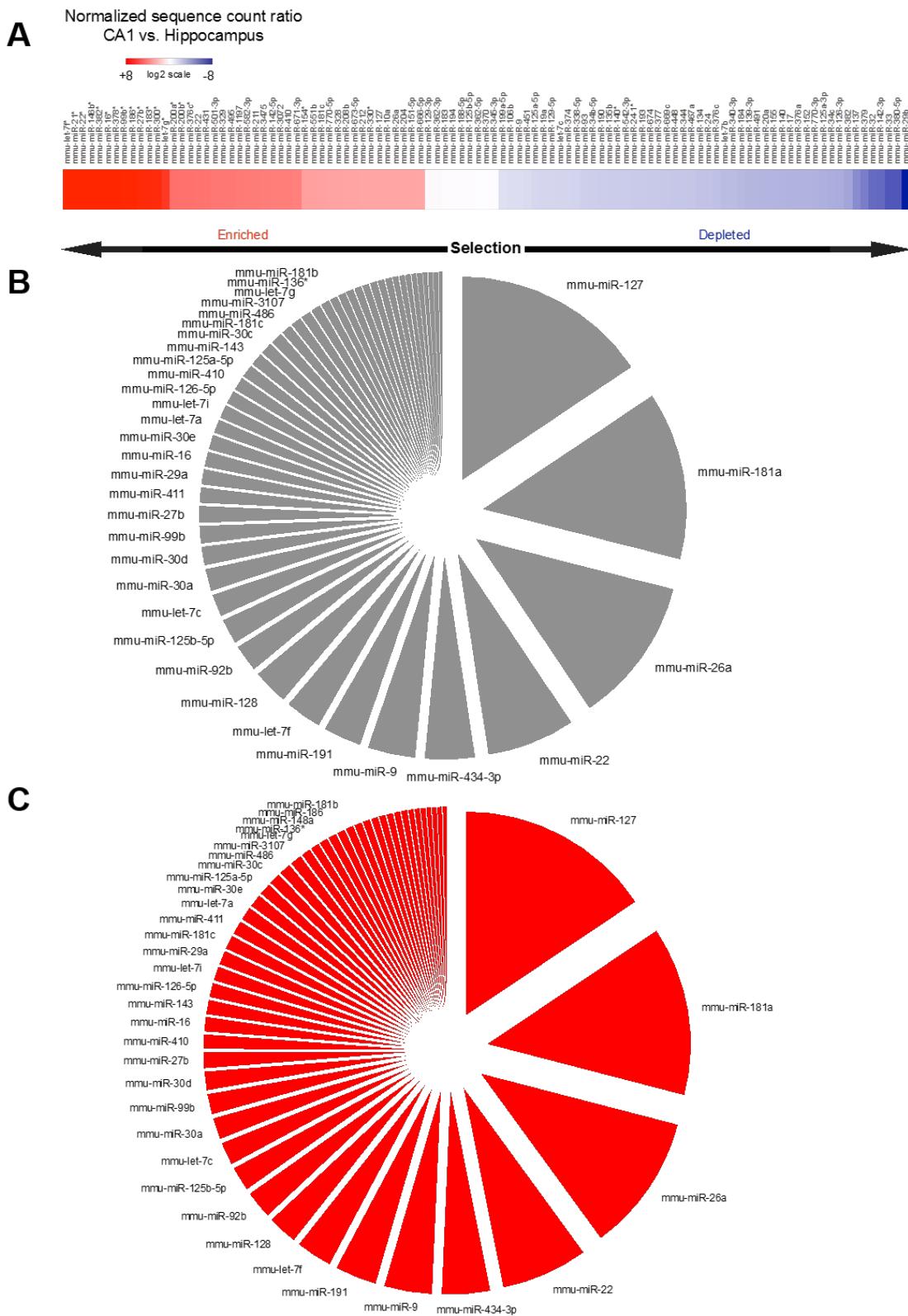
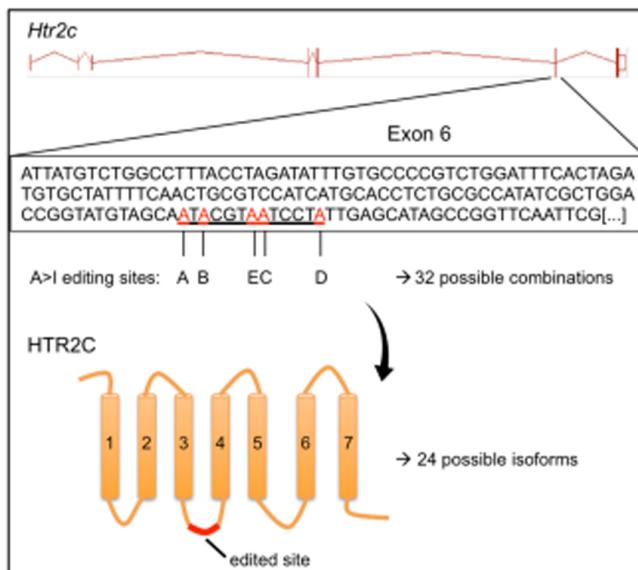


Figure S5. KAT2A does not regulate the CA1 microRNAome. **A.** Comparison of the miRNome of the whole hippocampus with the CA1-specific miRNome reported in this paper. **B-C.** Comparison of microRNA expression levels did not reveal any significant differences. Average distribution of normalized read counts of the Top50 microRNAs was similar between control (**C**) and *Kat2a* cKO (**C**) mice (n=6/group). For the full list and Top50 comparison see Table_S5.

Fig S6.

A



B

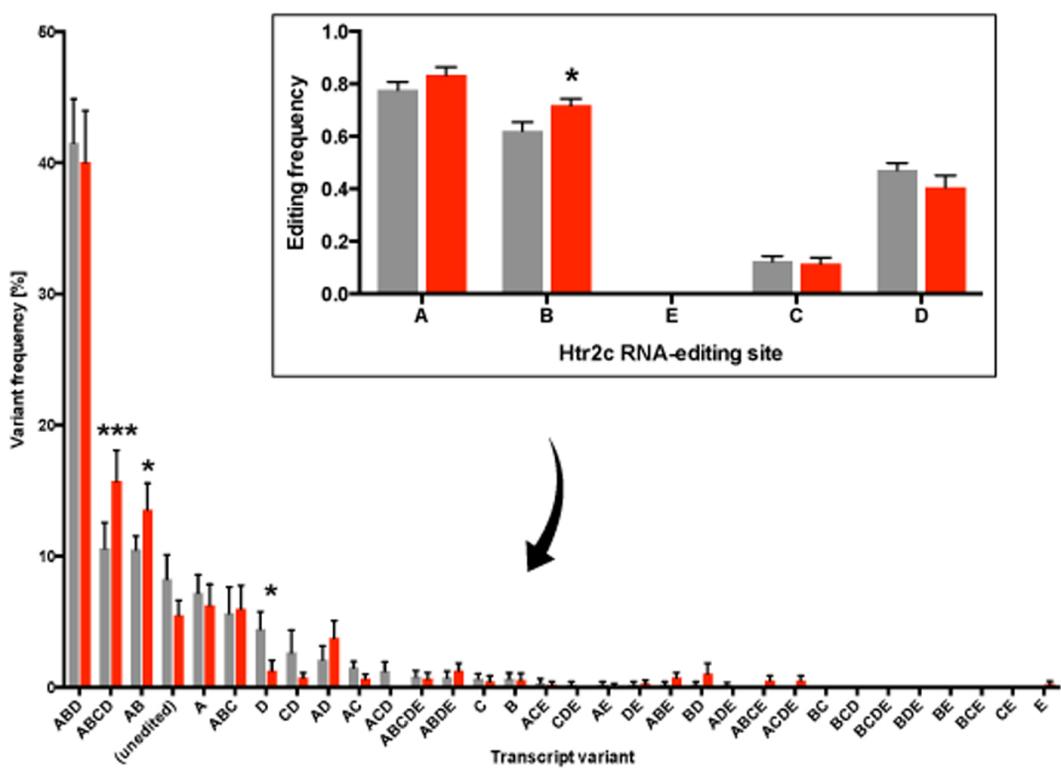


Fig. S6. Htr2c mRNA-editing is altered in *Kat2a* cKO mice

It is likely, that multiple KAT2a-dependent processes contribute to a phenotype that is a complex as memory formation. To address this issue – at least in part – we asked if *Kat2a* may be involved in other types of post-transcriptional or co-transcriptional modifications. In addition to the analysis of the transcriptome and the microRNAome we were able to employ our dataset to investigate RNA-editing at known sites.

A. The serotonin receptor HTR2C is known to be subject to well defined RNA-editing, a process in which adenosine bases in the transcribed mRNA are deaminated to inosine bases (A>I

modification) (Burns et al, 1997). As editing is occurring in the protein coding region (exon 6) of the *Htr2c* mRNA it leads to altered protein function (Burns et al, 1997). The image shows an overview of the mRNA-editing processing and edited sites in the *Htr2c* mRNA.

B. Using our RNA-seq dataset, we thus investigated the known modification to see whether RNA-editing of *Htr2c* mRNA is altered by loss of *Kat2a*. Using as similar read coverage over the exon 6 for *Kat2a* cKO and control mice we found a significant increase in editing frequency at the B site of the editing cassette that was due to an increase in the relative abundance of the ABCD-edited and AB-edited variants, which were the second- and third-most expressed variants in the CA1 (**Table S6**), and a decrease in the variant edited at the D site. This translates to an increase in the VSV- and VNI-protein isoforms and a decrease in the INV-protein isoform. Notably, an increased VNI- as well as the VSV-protein isoforms have been associated with decreased function of the HTR2C receptor, since the edited protein region is involved in G-Protein-coupling (Berg et al, 2008; Burns et al, 1997; Schellekens et al, 2012). Together with decreased overall expression of the *Htr2c* gene, this leads to further reduced HTR2C signaling in the CA1 region. In summary panel B shows that A>I editing at site B was significantly altered, which was due to increase of the ABCD- and AB-transcript variants and decrease in the D-transcript variant (n=11-13/group, Holm-Sidak-corrected multiple, two-sided t-tests, ***p<0.001, *p<0.05). Error bars represent S.E.M.

Discussion of the presented data: We were able to employ our dataset to investigate RNA-editing at known sites and found, that the *Htr2c* mRNA was edited to increase variant frequencies that are associated with compromised protein function. Since mRNA editing is occurring co-transcriptionally and before splicing (Bentley, 2014), we therefore speculate that loss of *Kat2a* and therefore decreased histone acetylation during transcription may lead to a decreased RNA-polII-dependent transcription rate, which leaves the editing enzymes (ADAR) with more time to carry out the necessary chemical reactions (Bentley, 2014) (Rodriguez et al, 2012).

Bentley DL (2014) Coupling mRNA processing with transcription in time and space. *Nat Rev Genet* 15: 163-175

Berg KA, Clarke WP, Cunningham KA, Spampinato U (2008) Fine-tuning serotonin2c receptor function in the brain: molecular and functional implications. *Neuropharmacology* 55: 969-976

Burns CM, Chu H, Rueter SM, Hutchinson LK, Canton H, Sanders-Bush E, Emeson RB (1997) Regulation of serotonin-2C receptor G-protein coupling by RNA editing. *Nature* 387: 303-308

Rodriguez J, Menet JS, Rosbash M (2012) Nascent-seq indicates widespread cotranscriptional RNA editing in Drosophila. *Mol Cell* 47: 27-37

Schellekens H, Clarke G, Jeffery IB, Dinan TG, Cryan JF (2012) Dynamic 5-HT2C receptor editing in a mouse model of obesity. *PLoS One* 7: e32266

Table S1. Genes expressed in hippocampal CA1 region**A. TOP50 genes expressed in CA1**

Ensembl Gene ID	MGI Symbol
ENSMUSG00000024617	Camk2a
ENSMUSG00000074657	Kif5a
ENSMUSG00000005089	Slc1a2
ENSMUSG00000001175	Calm1
ENSMUSG00000037852	Cpe
ENSMUSG00000027273	Snap25
ENSMUSG00000028161	Ppp3ca
ENSMUSG00000026576	Atp1b1
ENSMUSG00000029309	Sparcl1
ENSMUSG00000040907	Atp1a3
ENSMUSG00000021268	Meg3
ENSMUSG00000036438	Calm2
ENSMUSG00000098178	RP23-81C12.3
ENSMUSG00000041607	Mbp
ENSMUSG00000031517	Gpm6a
ENSMUSG00000037742	Eef1a1
ENSMUSG00000035864	Syt1
ENSMUSG00000022892	App
ENSMUSG00000023944	Hsp90ab1
ENSMUSG00000028833	Ncdn
ENSMUSG00000059213	Ddn
ENSMUSG00000031425	Plp1
ENSMUSG00000025867	Cplx2
ENSMUSG00000036564	Ndrg4
ENSMUSG0000004207	Psap
ENSMUSG00000030695	Aldoa
ENSMUSG00000015222	Map2
ENSMUSG00000051853	Arf3
ENSMUSG00000019943	Atp2b1
ENSMUSG00000019370	Calm3
ENSMUSG00000025203	Scd2
ENSMUSG00000057738	Sptan1
ENSMUSG00000024661	Fth1
ENSMUSG00000027254	Map1a
ENSMUSG00000014602	Kif1a
ENSMUSG00000044349	Snhg11
ENSMUSG00000024758	Rtn3
ENSMUSG00000032294	Pkm
ENSMUSG00000040785	Ttc3
ENSMUSG00000019877	Serinc1
ENSMUSG00000020431	Adcy1
ENSMUSG00000033981	Gria2
ENSMUSG00000046093	Hpcal4
ENSMUSG00000020524	Gria1
ENSMUSG00000025393	Atp5b

Functional annotation of Top50 expressed genes in mouse CA1 (from DESeq2 output)

red: terms associated with neuronal function

***: FDR<0.001; **:FDR<0.01; *:FDR<0.05; #:FDR<0.1

KEGG-Pathway Term	Fold Enrichment	PValue	FDR	Significant?
mmu04720:Long-term potentiation	21.4	4.9E-06	4.7E-05	***
mmu05014:Amyotrophic lateral sclerosis (ALS)	18.3	1.1E-03	1.0E-02	**
mmu04020:Calcium signaling pathway	6.9	4.4E-03	4.1E-02	*
mmu04114:Oocyte meiosis	8.8	8.6E-03	8.0E-02	#
mmu05010:Alzheimer's disease	5.9	2.5E-02	2.1E-01	ns.

GO Term	Fold Enrichment	PValue	FDR	Significant?
GO:0007268~synaptic transmission	11.1	1.4E-07	1.87E-06	***
GO:0006164~purine nucleotide biosynthetic process	13.5	6.6E-05	9.06E-04	***
GO:0009142~nucleoside triphosphate biosynthetic process	16.3	2.1E-04	2.94E-03	**
GO:0034404~nucleobase, nucleoside and nucleotide biosynthetic process	10.3	2.3E-04	3.15E-03	**
GO:0034654~nucleobase, nucleoside, nucleotide and nucleic acid biosynthetic process	10.3	2.3E-04	3.15E-03	**
GO:0007611~learning or memory	15.0	3.0E-04	4.07E-03	**
GO:0009144~purine nucleoside triphosphate metabolic process	13.6	4.3E-04	5.83E-03	**
GO:0009260~ribonucleotide biosynthetic process	13.4	4.5E-04	6.20E-03	**
GO:0007616~long-term memory	83.1	5.4E-04	7.40E-03	**
GO:0009150~purine ribonucleotide metabolic process	12.0	6.8E-04	9.27E-03	**
GO:0055082~cellular chemical homeostasis	6.1	7.4E-04	1.02E-02	*
GO:0006812~cation transport	4.8	9.6E-04	1.31E-02	*
GO:0050801~ion homeostasis	5.7	1.1E-03	1.49E-02	*
GO:0006753~nucleoside phosphate metabolic process	6.8	1.5E-03	2.08E-02	*
GO:0030001~metal ion transport	5.0	2.1E-03	2.85E-02	*
GO:0007632~visual behavior	32.1	3.7E-03	4.93E-02	*
GO:0043242~negative regulation of protein complex disassembly	24.3	6.4E-03	8.40E-02	#
GO:0050804~regulation of synaptic transmission	9.8	7.2E-03	9.50E-02	#

B. Pathway analysis of TOP 50 genes

Table S2: Differential expressed genes amongst KAT2A cKO and control mice in the CA1 region

Up(WT naive vs. novelty)		Down(WT naive vs. novelty)	
MGI Symbol	ENSEMBL-ID	MGI Symbol	ENSEMBL-ID
Egr2	ENSMUSG00000037868	AB041806	ENSMUSG00000046109
Fos	ENSMUSG00000021250	Aim1	ENSMUSG00000019866
Fosb	ENSMUSG00000003545	Egf	ENSMUSG00000028017
Egr1	ENSMUSG00000038418	Gm12908	ENSMUSG00000087200
Egr4	ENSMUSG00000071341	Dcaf12i2	ENSMUSG00000050926
1700016P03Rik	ENSMUSG00000085609	Tlr9	ENSMUSG00000045322
Maff	ENSMUSG00000042622	Tmem194b	ENSMUSG00000043015
Fam83d	ENSMUSG00000027654	Samsn1	ENSMUSG00000022876
Nr4a1	ENSMUSG00000023034	Gm5577	ENSMUSG00000084950
Homer1	ENSMUSG00000007617	A2m	ENSMUSG00000030111
Arc	ENSMUSG00000022602	Adrb3	ENSMUSG00000031489
Dusp5	ENSMUSG00000034765	Klhdc9	ENSMUSG00000045259
Sik1	ENSMUSG00000024042	BC024139	ENSMUSG00000044361
Arl4d	ENSMUSG00000034936	Edn1	ENSMUSG00000021367
Plekhf1	ENSMUSG00000074170	Micall2	ENSMUSG00000036718
Nr4a3	ENSMUSG00000028341	Tnfsf10	ENSMUSG00000039304
Sgk1	ENSMUSG00000019970	Apobec1	ENSMUSG00000040613
Per1	ENSMUSG00000020893	Hhex	ENSMUSG00000024986
Egr3	ENSMUSG00000033730	Ccno	ENSMUSG00000042417
Nostrin	ENSMUSG00000034738	Gprc5c	ENSMUSG00000051043
Fas	ENSMUSG00000024778	Heyl	ENSMUSG00000032744
Cdkn1a	ENSMUSG00000023067	RP23-285C18.2	ENSMUSG00000097415
Tsc22d3	ENSMUSG00000031431	Rassf9	ENSMUSG00000044921
Dio2	ENSMUSG0000007682	Pabpc4l	ENSMUSG00000090919
Arid5a	ENSMUSG00000037447	Pcdhb1	ENSMUSG00000051663
Junb	ENSMUSG00000052837	Gm11948	ENSMUSG00000087055
Fam46a	ENSMUSG00000032265	Irs4	ENSMUSG00000054667
Ppp1r3g	ENSMUSG00000050423	Fam181a	ENSMUSG00000096753
Errfi1	ENSMUSG00000028967	Cd180	ENSMUSG00000021624
Klf2	ENSMUSG00000055148	Gm20692	ENSMUSG00000093739
Mc4r	ENSMUSG00000047259	G530011O06Rik	ENSMUSG00000072844
Nr4a2	ENSMUSG00000026826	Klhl6	ENSMUSG00000043008
Fhl3	ENSMUSG00000032643		
Fosl2	ENSMUSG00000029135		
Map3k19	ENSMUSG00000051590		
Rasd1	ENSMUSG00000049892		
Fam150b	ENSMUSG00000054204		
Tiparp	ENSMUSG00000034640		
Xdh	ENSMUSG00000024066		
Gadd45b	ENSMUSG00000015312		
Arl5b	ENSMUSG00000017418		
Sertad1	ENSMUSG00000008384		
Prr5	ENSMUSG00000036106		
Gpr3	ENSMUSG00000049649		
Utp14b	ENSMUSG00000079470		
Zdbf2	ENSMUSG00000027520		
Spsb1	ENSMUSG00000039911		
Dusp6	ENSMUSG00000019960		
Jhdm1d	ENSMUSG00000042599		
Plin4	ENSMUSG00000028321		
Coq10b	ENSMUSG00000025981		
Gpt2	ENSMUSG00000031700		

Tnfrsf12a	ENSMUSG00000023905
Dnajb5	ENSMUSG00000036052
Adipor2	ENSMUSG00000030168
Nptx2	ENSMUSG00000059991
Mettl11b	ENSMUSG00000040113
Per2	ENSMUSG00000055866
Pcsk1	ENSMUSG00000021587
Lingo3	ENSMUSG00000051067
Nfkbia	ENSMUSG00000021025
Mfsd2a	ENSMUSG00000028655
Irs2	ENSMUSG00000038894
Zfp189	ENSMUSG00000039634
Dnajb1	ENSMUSG00000005483
Smim3	ENSMUSG00000038059
Midn	ENSMUSG00000035621
Slc2a1	ENSMUSG00000028645
Klf15	ENSMUSG00000030087
Rrp8	ENSMUSG00000030888
Rasl11b	ENSMUSG00000049907
Ier5	ENSMUSG00000056708
Dusp4	ENSMUSG00000031530
Lrmp	ENSMUSG00000030263
Zfp319	ENSMUSG00000074140

Up(WT naive vs. Kat2a cKO naive)		Down(WT naive vs. Kat2a cKO naive)	
MGFI Symbol	ENSEMBL-ID	MGFI Symbol	ENSEMBL-ID
Klk10	ENSMUSG00000030693	Pcdhb4	ENSMUSG00000045689
Otop2	ENSMUSG00000050201	Akr1c14	ENSMUSG00000033715
Cdhr1	ENSMUSG00000021803	Htr2c	ENSMUSG00000041380
Cacng6	ENSMUSG00000078815	Col11a1	ENSMUSG00000027966
Ano2	ENSMUSG00000038115	Hcrtr2	ENSMUSG00000032360
B3gnt8	ENSMUSG00000059479	Gm12198	ENSMUSG00000085564
Baiap3	ENSMUSG00000047507	A530058N18Rik	ENSMUSG00000087694
Sec14l4	ENSMUSG00000019368	5430416O09Rik	ENSMUSG00000028475
Tbxa2r	ENSMUSG00000034881	Spink10	ENSMUSG00000044176
Plb1	ENSMUSG00000029134	Irak3	ENSMUSG00000020227
Adamts18	ENSMUSG00000053399	Zfp934	ENSMUSG00000074865
Pstpip1	ENSMUSG00000032322	Npbwr1	ENSMUSG00000033774
Trpa1	ENSMUSG00000032769	Ghsr	ENSMUSG00000051136
Cpxm2	ENSMUSG00000030862	Atp4a	ENSMUSG00000005553
Tgm3	ENSMUSG00000027401	Gm5815	ENSMUSG00000046952
Trp73	ENSMUSG00000029026	G530011O06Rik	ENSMUSG00000072844
Ush1g	ENSMUSG00000045288	2310042E22Rik	ENSMUSG00000090356
P2rx5	ENSMUSG00000005950	Cyp26b1	ENSMUSG00000063415
Rspo1	ENSMUSG00000028871	AC140785.1	ENSMUSG00000097869
Cldn26	ENSMUSG00000022715	Adcyap1	ENSMUSG00000024256
Crabp2	ENSMUSG00000004885	Penk	ENSMUSG00000045573
Igfbpl1	ENSMUSG00000035551	2410018L13Rik	ENSMUSG00000073164
Loxl1	ENSMUSG00000032334	Kat2a	ENSMUSG00000020918
Zfp296	ENSMUSG00000011267	Grem1	ENSMUSG00000074934
Epor	ENSMUSG0000006235	Oxr1	ENSMUSG00000022307
Gm9821	ENSMUSG00000095332		
Medag	ENSMUSG00000029659		
Clca2	ENSMUSG00000028262		
Tjp3	ENSMUSG00000034917		
Cd163	ENSMUSG0000008845		
Jsrp1	ENSMUSG00000020216		

RP23-42D10.1	ENSMUSG00000098072
Gm4737	ENSMUSG00000048087
Atp2c2	ENSMUSG00000034112
Itgb7	ENSMUSG0000001281
Crlf1	ENSMUSG00000007888
Smtnl2	ENSMUSG00000045667
Zfp185	ENSMUSG00000031351
Clspn	ENSMUSG00000042489
Kcne3	ENSMUSG00000035165
RP24-158L2.1	ENSMUSG00000098097
Pgpep1l	ENSMUSG00000030553
Ucma	ENSMUSG00000026668
Vwa3a	ENSMUSG00000030889
Epn3	ENSMUSG00000010080
Adamts13	ENSMUSG00000014852
Rhcg	ENSMUSG00000030549
Gm15860	ENSMUSG00000087336
A630023P12Rik	ENSMUSG00000048215
Ccdc129	ENSMUSG00000037973
Sypl2	ENSMUSG00000027887
Diap3	ENSMUSG00000022021
Myo1h	ENSMUSG00000066952
Rreb1	ENSMUSG00000039087
Otogl	ENSMUSG00000091455
RP24-413G2.4	ENSMUSG00000098128
Myh3	ENSMUSG00000020908
Col22a1	ENSMUSG00000079022
Igdcc3	ENSMUSG00000032394
Mapk12	ENSMUSG00000022610
Dkk1l	ENSMUSG00000030792
Serpinc1	ENSMUSG00000023224
Slc29a1	ENSMUSG00000023942
Ttc22	ENSMUSG00000034919
Ppl	ENSMUSG00000039457
Gck	ENSMUSG00000041798
Hbb-b1	ENSMUSG00000052305
Slc26a8	ENSMUSG00000036196
Fam160a1	ENSMUSG00000051000
Blnk	ENSMUSG00000061132
Spint1	ENSMUSG00000027315

Up(WT novelty vs. *Kat2a* cKO novelty)

MGI Symbol	ENSEMBL-ID
Tbx2r	ENSMUSG00000034881
Baiap3	ENSMUSG00000047507
Capn11	ENSMUSG00000058626
Cldn26	ENSMUSG00000022715
Trp73	ENSMUSG00000029026
RP23-42D10.1	ENSMUSG00000098072
Tacr2	ENSMUSG00000020081
Ush1g	ENSMUSG00000045288
Cdhr1	ENSMUSG00000021803
Spn	ENSMUSG00000051457
B3gnt8	ENSMUSG00000059479
Itgb7	ENSMUSG00000001281
Col6a5	ENSMUSG00000091345
BC024139	ENSMUSG00000044361

Down(WT novelty vs. *Kat2a* cKO novelty)

MGI Symbol	ENSEMBL-ID
Eva1c	ENSMUSG00000039903
AC129605.1	ENSMUSG00000097789
Plekhg1	ENSMUSG00000040624
Mmrn2	ENSMUSG00000041445
Igfbp4	ENSMUSG00000017493
Gm15710	ENSMUSG00000084111
Gm15631	ENSMUSG00000085067
Ddn	ENSMUSG00000059213
Sema3a	ENSMUSG00000028883
Zfp97	ENSMUSG00000095990
Akr1c14	ENSMUSG00000033715
Rpl9-ps7	ENSMUSG00000047965
Aldh1a1	ENSMUSG00000053279
Oprk1	ENSMUSG00000025905

Klk10	ENSMUSG00000030693	Scn3b	ENSMUSG00000049281
Cacng6	ENSMUSG00000078815	Htr2a	ENSMUSG00000034997
AC145610.1	ENSMUSG00000097593	Htr1a	ENSMUSG00000021721
Col6a2	ENSMUSG00000020241	Akr1c18	ENSMUSG00000021214
Pstpip1	ENSMUSG00000032322	Coch	ENSMUSG00000020953
A2m	ENSMUSG00000030111	Stac	ENSMUSG00000032502
Otof	ENSMUSG00000062372	Rpl9-ps4	ENSMUSG00000094989
Cd109	ENSMUSG00000046186	Gm3667	ENSMUSG00000090691
Gm15422	ENSMUSG00000082738	Myl4	ENSMUSG00000061086
Plb1	ENSMUSG00000029134	Gm10012	ENSMUSG00000057580
Ucma	ENSMUSG00000026668	Scn4b	ENSMUSG00000046480
Ano2	ENSMUSG00000038115	Fam19a1	ENSMUSG00000059187
Xpnpep2	ENSMUSG00000037005	Gm10029	ENSMUSG00000068324
Clca1	ENSMUSG00000056025	Unc13c	ENSMUSG00000062151
Spata18	ENSMUSG00000029155	Meox1	ENSMUSG00000001493
Olfm4	ENSMUSG00000022026	AC164597.1	ENSMUSG00000097493
Gm15478	ENSMUSG00000085363	Mc4r	ENSMUSG00000047259
Dnahc11	ENSMUSG00000018581	Apln	ENSMUSG00000037010
RP24-158L2.1	ENSMUSG00000098097	Npbwr1	ENSMUSG00000033774
Mfap4	ENSMUSG00000042436	Htr1b	ENSMUSG00000049511
Epn3	ENSMUSG00000010080	Plekha2	ENSMUSG00000031557
Gm9821	ENSMUSG00000095332	Gm11263	ENSMUSG00000083496
Wdr66	ENSMUSG00000029442	Adcyap1	ENSMUSG00000024256
Epb4.1l4a	ENSMUSG00000024376	Lefty1	ENSMUSG00000038793
Scn7a	ENSMUSG00000034810	Gm15721	ENSMUSG00000085565
5330416C01Rik	ENSMUSG00000054944	Htra4	ENSMUSG00000037406
Igdcc3	ENSMUSG00000032394	Slc35d3	ENSMUSG00000050473
Thbs3	ENSMUSG00000028047	Gm17732	ENSMUSG00000091744
Llg12	ENSMUSG00000020782	Fam83d	ENSMUSG00000027654
Gm11721	ENSMUSG00000087064	Gm4613	ENSMUSG00000090467
Scube2	ENSMUSG00000007279	Rps3a3	ENSMUSG00000059751
Hydin	ENSMUSG00000059854	Cyp26b1	ENSMUSG00000063415
Ifi203	ENSMUSG00000039997	Spink10	ENSMUSG00000044176
Ccdc153	ENSMUSG00000070306	Ghsr	ENSMUSG00000051136
Tex15	ENSMUSG00000009628	Ninj2	ENSMUSG00000041377
Ccdc88b	ENSMUSG00000047810	Slitrk6	ENSMUSG00000045871
Ppp2r3d	ENSMUSG00000093803	Cdk15	ENSMUSG00000026023
Cdsn	ENSMUSG00000039518	Kat2a	ENSMUSG00000020918
Myo1h	ENSMUSG00000066952	C1ql2	ENSMUSG00000036907
Pou6f2	ENSMUSG00000009734	Grem1	ENSMUSG00000074934
Ybx2	ENSMUSG00000018554	Penk	ENSMUSG00000045573
Zglp1	ENSMUSG00000079681	Oxr1	ENSMUSG00000022307
1700040L02Rik	ENSMUSG00000019945	2410018L13Rik	ENSMUSG00000073164
Adamts14	ENSMUSG00000059901		
Best3	ENSMUSG00000020169		
Rreb1	ENSMUSG00000039087		
Tjp3	ENSMUSG00000034917		
Col5a3	ENSMUSG00000004098		
Gm4779	ENSMUSG00000045010		
Igfbpl1	ENSMUSG00000035551		
Zfp185	ENSMUSG00000031351		
Lpar5	ENSMUSG00000067714		
Papln	ENSMUSG00000021223		
Ccno	ENSMUSG00000042417		
Bcl2l15	ENSMUSG00000044165		
Lpar2	ENSMUSG00000031861		
Tnni3k	ENSMUSG00000040086		

Iqub	ENSMUSG00000046192
Ccdc162	ENSMUSG00000075225
Loxl1	ENSMUSG00000032334
AC152181.1	ENSMUSG00000097259
Derl3	ENSMUSG00000009092
Aldh1a3	ENSMUSG00000015134
Gm216	ENSMUSG00000073650
Vwa3a	ENSMUSG00000030889
Pgpep1l	ENSMUSG00000030553
Figf	ENSMUSG00000031380
Sec16b	ENSMUSG00000026589
Gm16119	ENSMUSG00000010492
Dnaaf3	ENSMUSG00000055809
Zfp296	ENSMUSG00000011267
Fxyd2	ENSMUSG00000059412
Medag	ENSMUSG00000029659
Gm7120	ENSMUSG00000074634
Catsperg1	ENSMUSG00000049676
Tacr1	ENSMUSG00000030043
1700026D08Rik	ENSMUSG00000011154
Otogl	ENSMUSG00000091455
Gm8261	ENSMUSG00000081718
Anxa1	ENSMUSG00000024659
Hpn	ENSMUSG00000001249
Gm15423	ENSMUSG00000087082
Kcnh6	ENSMUSG00000001901
Slc26a8	ENSMUSG00000036196
Mcm10	ENSMUSG00000026669
Ngb	ENSMUSG00000021032
Adamts13	ENSMUSG00000014852
Fam179a	ENSMUSG00000045761
Sypl2	ENSMUSG00000027887
Ryr1	ENSMUSG00000030592
Pygl	ENSMUSG00000021069
Ppl	ENSMUSG00000039457
6820408C15Rik	ENSMUSG00000032680
Xrra1	ENSMUSG00000035211
RP24-413G2.4	ENSMUSG00000098128
Acy3	ENSMUSG00000024866
Rln1	ENSMUSG00000039097
Ptpn14	ENSMUSG00000026604
Aloxe3	ENSMUSG00000020892
Epor	ENSMUSG00000006235
AC149052.1	ENSMUSG00000097246
Nbeal2	ENSMUSG00000056724
Gm867	ENSMUSG00000050157
Gm5577	ENSMUSG00000084950
Atg9b	ENSMUSG00000038295
Ccdc155	ENSMUSG00000038292
AC122200.1	ENSMUSG00000097133
Sebox	ENSMUSG00000001103
Cpxm2	ENSMUSG00000030862
Hes5	ENSMUSG00000048001
Tmem181c-ps	ENSMUSG00000093880
Ccl28	ENSMUSG00000074715
Unc13d	ENSMUSG00000057948
Serpingle1	ENSMUSG00000023224

Col6a1	ENSMUSG00000001119
Dnase1l2	ENSMUSG00000024136
Fbxo48	ENSMUSG00000044966
Ankrd53	ENSMUSG00000014747
Fndc9	ENSMUSG00000048721
Gm14137	ENSMUSG00000055926
Gm10658	ENSMUSG00000074284
Fam117a	ENSMUSG00000038893
Crybb3	ENSMUSG00000029352
Crocc	ENSMUSG00000040860
Dock6	ENSMUSG00000032198
Rcor2	ENSMUSG00000024968
Pnck	ENSMUSG00000002012
Mxd3	ENSMUSG00000021485
Ccdc3	ENSMUSG00000026676
Homer3	ENSMUSG00000003573
Tm6sf2	ENSMUSG00000036151
1700016P03Rik	ENSMUSG00000085609
Fam183b	ENSMUSG00000049154
Kif27	ENSMUSG00000060176
Zfp57	ENSMUSG00000036036
Trpc7	ENSMUSG00000021541
Fam167a	ENSMUSG00000035095
Kcp	ENSMUSG00000059022
Strc	ENSMUSG00000033498
Rnf207	ENSMUSG00000058498
Atoh8	ENSMUSG00000037621
Blnk	ENSMUSG00000061132
Scarf2	ENSMUSG00000012017
Magel2	ENSMUSG00000056972
Gm15567	ENSMUSG00000084974
Slc16a11	ENSMUSG00000040938
Tonsl	ENSMUSG00000059323
1700019L03Rik	ENSMUSG00000038987

Up(*Kat2a* cKO naive vs. novelty)

MGI Symbol	ENSEMBL-ID
Egr2	ENSMUSG00000037868
Fosb	ENSMUSG00000003545
Fos	ENSMUSG00000021250
1700016P03Rik	ENSMUSG00000085609
Egr1	ENSMUSG00000038418
Egr4	ENSMUSG00000071341
Mir132	ENSMUSG00000065537
Homer1	ENSMUSG00000007617
Arc	ENSMUSG00000022602
Nr4a1	ENSMUSG00000023034
Sik1	ENSMUSG00000024042
Fosl2	ENSMUSG00000029135
Nr4a3	ENSMUSG00000028341
Fam46a	ENSMUSG00000032265
Dusp5	ENSMUSG00000034765
RP23-204I16.2	ENSMUSG00000098061
Junb	ENSMUSG00000052837
Fam150b	ENSMUSG00000054204
Egr3	ENSMUSG00000033730
Maff	ENSMUSG00000042622

Down(*Kat2a* cKO naive vs. novelty)

MGI Symbol	ENSEMBL-ID
Adamts18	ENSMUSG00000053399
Oacyl	ENSMUSG00000046610
Clec2d	ENSMUSG00000030157
Ehhadh	ENSMUSG00000022853
Gm6970	ENSMUSG00000091230
9930012K11Rik	ENSMUSG00000044551
Nkx3-1	ENSMUSG00000022061
Mamstr	ENSMUSG00000042918
Tnfsf10	ENSMUSG00000039304
Gm20633	ENSMUSG00000093553
Plekho2	ENSMUSG00000050721
Pkdrej	ENSMUSG00000052496
Rbm46	ENSMUSG00000033882
Rnf138rt1	ENSMUSG00000083695
Col22a1	ENSMUSG00000079022
Clspn	ENSMUSG00000042489
0610040B10Rik	ENSMUSG00000089889
Gm12178	ENSMUSG00000081952
Cd180	ENSMUSG00000021624

Tnfrsf25	ENSMUSG00000024793
Zglp1	ENSMUSG00000079681
Rtp1	ENSMUSG00000033383
Atoh8	ENSMUSG00000037621
8430408G22Rik	ENSMUSG00000048489
Tm6sf2	ENSMUSG00000036151
Gpr3	ENSMUSG00000049649
Map3k19	ENSMUSG00000051590
Zdbf2	ENSMUSG00000027520
Agxt2I1	ENSMUSG00000019232
Dnase1I2	ENSMUSG00000024136
Plekhf1	ENSMUSG00000074170
Per1	ENSMUSG00000020893
Gadd45b	ENSMUSG00000015312
Nr4a2	ENSMUSG00000026826
Sgk1	ENSMUSG00000019970
Plin4	ENSMUSG00000002831
Cdkn1a	ENSMUSG00000023067
Gm11201	ENSMUSG00000085941
Gem	ENSMUSG00000028214
Dusp6	ENSMUSG00000019960
1810011O10Rik	ENSMUSG00000056313
Noxred1	ENSMUSG00000072919
Errfi1	ENSMUSG00000028967
Arl5b	ENSMUSG00000017418
Crip3	ENSMUSG00000023968
Tiparp	ENSMUSG00000034640
Ankrd53	ENSMUSG00000014747
Rasl11a	ENSMUSG00000029641
Utp14b	ENSMUSG00000079470
Nfil3	ENSMUSG00000056749
Tsc22d3	ENSMUSG00000031431
Midn	ENSMUSG00000035621
Coq10b	ENSMUSG00000025981
Arl4d	ENSMUSG00000034936
1700102P08Rik	ENSMUSG00000032611
Fas	ENSMUSG00000024778
Dio2	ENSMUSG00000007682
Arid5a	ENSMUSG00000037447
Per2	ENSMUSG00000055866
Mlph	ENSMUSG00000026303
Bag3	ENSMUSG00000030847
Hpn	ENSMUSG00000001249
Irs2	ENSMUSG00000038894
Plk3	ENSMUSG00000028680
Mir374	ENSMUSG00000076269
Dnajb1	ENSMUSG00000005483
Jhdm1d	ENSMUSG00000042599
Gm15478	ENSMUSG00000085363
Sertad1	ENSMUSG00000008384
Dusp1	ENSMUSG00000024190
Spry4	ENSMUSG00000024427
Gpt2	ENSMUSG00000031700
Acer2	ENSMUSG00000038007
Dnajb5	ENSMUSG00000036052
Chrm4	ENSMUSG00000040495
A930039A15Rik	ENSMUSG00000078493

Nptx2	ENSMUSG00000059991
Gm13502	ENSMUSG00000083287
Dok3	ENSMUSG00000035711
Pcsk1	ENSMUSG00000021587
P4ha1	ENSMUSG00000019916
Hspb1	ENSMUSG00000004951
Zswim6	ENSMUSG00000032846
Klf2	ENSMUSG0000005148
Fastkd5	ENSMUSG00000079043
Gm13830	ENSMUSG00000086368
Uba6	ENSMUSG00000035898
Spata2l	ENSMUSG00000033594
Ppp1r3g	ENSMUSG00000050423

Table S3: Pathway analysis on differentially expressed genes.

While MAPK signaling was normally induced in *Kat2a* cKO mice, genes functioning in “neuroactive ligand-receptor interaction” were commonly significantly enriched among down-regulated genes in the CA1 of *Kat2a* cKO mice. Genes selected for subsequent qPCR analysis are marked in **bold**.

		Up	<i>No enriched pathway found</i>			-
WT vs. <i>Kat2a</i> cKO naïve	Down	Neuroactive ligand-receptor interaction	4.3E-3	2.6E-2	<i>Htr2c, Ghsr, Hcrtr2, Npbwr1</i>	
	All	Neuroactive ligand-receptor interaction	3.8E-3	3.6E-2	<i>Htr2c, Ghsr, Hcrtr2, Npbwr1, P2rx5, Tbx2r</i>	
	Up	MAPK signaling pathway Adipocytokine signaling pathway	1.5E-4 1.3E-3	1.4E-3 1.2E-2	<i>Fas, Fos, Dusp4, Dusp5, Dusp6, Gadd45b, Nr4a1</i> <i>Adipor2, Irs2, Nfkbia, Slc2a1</i>	
WT naïve vs. novelty	Down	<i>No enriched pathway found</i>				-
	All	MAPK signaling pathway Adipocytokine signaling pathway	1.7E-4 2.4E-4	1.6E-3 2.4E-3	<i>Fas, Fos, Dusp4, Dusp5, Dusp6, Nr4a, Egf, Gadd45b</i> <i>Adipor2, Irs2, Irs4, Nfkbia, Slc2a1</i>	
	Up	MAPK signaling pathway	1.9E-5	1.7E-4	<i>Fas, Fos, Dusp1, Dusp5, Dusp6, Nr4a1, Gadd45b, Hspb1</i>	
<i>Kat2a</i> cKO naïve vs. novelty	Down	<i>No enriched pathway found</i>				-
	All	MAPK signaling pathway	5.4E-5	5.1E-4	<i>Fas, Fos, Dusp1, Dusp5, Dusp6, Nr4a1, Gadd45b, Hspb1, Il1a</i>	
	Up	ECM-receptor interaction Focal adhesion	6.4E-4 2.3E-3	5.9E-3 2.2E-2	<i>Col5a3, Col6a1, Col6a2, Itgb7, Thbs3, Figr</i>	
WT novelty vs. <i>Kat2a</i> cKO novelty	Down	Neuroactive ligand-receptor interaction	4.5E-5	2.8E-4	<i>Htr1a, Htr1b, Htr2a, Ghsr, Mc4r, Npbwr1, Oprk1</i>	
	All	Neuroactive ligand-receptor interaction ECM-receptor interaction	2.4E-5 3.9E-3	2.3E-4 3.6E-2	<i>Htr1a, Htr1b, Htr2a, Ghsr, Lpar2, Mc4r, Npbwr1, Oprk1, Tacr1, Tacr2, Tbx2r</i> <i>Col5a3, Col6a1, Col6a2, Itgb7, Thbs3</i>	

Table S4: miRNome of the mouse CA1 region ranked by normalized readcount

No significant differences were observed between control and Kat2a cKO mice (n=6). There are slight but non-significant changes in the order of the Top50-ranked (**bold**) miRNAs

<u>Rank</u>	<u>All miRNAs >10 reads (from controls)</u>	<u>Kat2a cKO</u>
1	mmu-miR-127	mmu-miR-127
2	mmu-miR-181a	mmu-miR-181a
3	mmu-miR-26a	mmu-miR-26a
4	mmu-miR-22	mmu-miR-22
5	mmu-miR-434-3p	mmu-miR-434-3p
6	mmu-miR-9	mmu-miR-9
7	mmu-miR-191	mmu-miR-191
8	mmu-let-7f	mmu-let-7f
9	mmu-miR-128	mmu-miR-128
10	mmu-miR-92b	mmu-miR-92b mmu-miR-125b-
11	mmu-miR-125b-5p	5p
12	mmu-let-7c	mmu-let-7c
13	mmu-miR-30a	mmu-miR-30a
14	mmu-miR-30d	mmu-miR-99b
15	mmu-miR-99b	mmu-miR-30d
16	mmu-miR-27b	mmu-miR-27b
17	mmu-miR-411	mmu-miR-410
18	mmu-miR-29a	mmu-miR-16
19	mmu-miR-16	mmu-miR-143
20	mmu-miR-30e	mmu-miR-126-5p
21	mmu-let-7a	mmu-let-7i
22	mmu-let-7i	mmu-miR-29a
23	mmu-miR-126-5p	mmu-miR-181c
24	mmu-miR-410	mmu-miR-411
25	mmu-miR-125a-5p	mmu-let-7a
26	mmu-miR-143	mmu-miR-30e mmu-miR-125a-
27	mmu-miR-30c	5p
28	mmu-miR-181c	mmu-miR-30c
29	mmu-miR-486	mmu-miR-486
30	mmu-miR-3107	mmu-miR-3107
31	mmu-let-7g	mmu-let-7g
32	mmu-miR-136*	mmu-miR-136*
33	mmu-miR-181b	mmu-miR-148a
34	mmu-miR-151-5p	mmu-miR-186
35	mmu-miR-186	mmu-miR-181b
36	mmu-miR-541	mmu-miR-151-3p
37	mmu-miR-151-3p	mmu-miR-103
38	mmu-miR-148a	mmu-miR-151-5p
39	mmu-miR-103	mmu-miR-132
40	mmu-miR-138	mmu-miR-138
41	mmu-miR-381	mmu-miR-541

42	mmu-miR-132	mmu-miR-381
43	mmu-miR-204	mmu-miR-204
44	mmu-miR-218	mmu-miR-100
45	mmu-let-7d	mmu-miR-26b
46	mmu-let-7b	mmu-miR-218
47	mmu-miR-101a	mmu-miR-101a
48	mmu-miR-338-3p	mmu-let-7d
49	mmu-miR-153	mmu-let-7b
50	mmu-miR-300	mmu-miR-92a
51	mmu-miR-100	mmu-miR-99a
52	mmu-miR-26b	mmu-miR-338-3p
53	mmu-miR-92a	mmu-miR-153
54	mmu-miR-222	mmu-miR-300
55	mmu-let-7e	mmu-let-7e
56	mmu-miR-99a	mmu-miR-21
57	mmu-miR-434-5p	mmu-miR-328
58	mmu-miR-21	mmu-miR-192
59	mmu-miR-192	mmu-miR-378
60	mmu-miR-328	mmu-miR-222
61	mmu-miR-221	mmu-miR-434-5p
62	mmu-miR-30b	mmu-miR-30b
63	mmu-miR-136	mmu-miR-340-5p
64	mmu-miR-378	mmu-miR-744
65	mmu-miR-744	mmu-miR-221
66	mmu-miR-340-5p	mmu-miR-136
67	mmu-miR-29c	mmu-miR-146b
68	mmu-miR-409-3p	mmu-miR-148b
69	mmu-miR-146b	mmu-miR-150
70	mmu-miR-126-3p	mmu-miR-29c
71	mmu-miR-301a	mmu-miR-301a
72	mmu-miR-148b	mmu-miR-126-3p
73	mmu-miR-150	mmu-miR-409-3p
74	mmu-miR-330	mmu-miR-330
75	mmu-miR-9*	mmu-miR-181d
76	mmu-miR-369-5p	mmu-miR-98
77	mmu-miR-98	mmu-miR-9*
78	mmu-miR-181d	mmu-miR-24
79	mmu-miR-23b	mmu-miR-30e*
80	mmu-miR-433	mmu-miR-107
81	mmu-miR-30e*	mmu-miR-1843b-5p
82	mmu-miR-149	mmu-miR-23b
83	mmu-miR-24	mmu-miR-149
84	mmu-miR-342-3p	mmu-miR-342-3p
85	mmu-miR-1843b-5p	mmu-miR-1843-5p
86	mmu-miR-107	mmu-miR-101b
87	mmu-miR-181a-1*	mmu-miR-139-5p
88	mmu-miR-129-5p	mmu-miR-369-5p
89	mmu-miR-487b	mmu-let-7d*
90	mmu-miR-34c	mmu-miR-129-5p

91	mmu-miR-125b-2-3p	mmu-miR-181a-1*
92	mmu-miR-139-5p	mmu-miR-433
93	mmu-let-7d*	mmu-miR-125b-2-3p
94	mmu-miR-3065	mmu-miR-488
95	mmu-miR-1843-5p	mmu-miR-1839-5p
96	mmu-miR-101b	mmu-miR-487b
97	mmu-miR-488	mmu-miR-341
98	mmu-miR-341	mmu-miR-212-5p
99		mmu-miR-129-2-3p
100	mmu-miR-344d	mmu-miR-344d
101	mmu-miR-384-5p	mmu-miR-212-3p
102	mmu-miR-129-2-3p	mmu-miR-425
103	mmu-miR-1839-5p	mmu-miR-3065
104	mmu-miR-425	mmu-miR-25
105	mmu-miR-212-3p	mmu-miR-130a
106	mmu-miR-212-5p	mmu-miR-384-5p
107	mmu-miR-708*	mmu-miR-30a*
108	mmu-miR-376b*	mmu-miR-23a
109	mmu-miR-380-3p	mmu-miR-708*
110	mmu-miR-30a*	mmu-miR-195
111	mmu-miR-130a	mmu-miR-1249
112	mmu-miR-872	mmu-miR-34c
113	mmu-miR-132*	mmu-miR-484
114	mmu-miR-195	mmu-miR-872
115	mmu-miR-668	mmu-miR-132*
116	mmu-miR-484	mmu-miR-380-3p
117	mmu-miR-1249	mmu-miR-335-3p
118	mmu-miR-25	mmu-miR-668
119	mmu-miR-219-3p	mmu-miR-497
120	mmu-miR-335-3p	mmu-miR-181c*
121	mmu-miR-879	mmu-miR-532-5p
122	mmu-miR-23a	mmu-miR-376b*
123	mmu-miR-146a	mmu-miR-879
124	mmu-miR-361	mmu-miR-361
125	mmu-miR-497	mmu-miR-598
126	mmu-miR-181c*	mmu-miR-29b
127	mmu-miR-29b	mmu-miR-146a
128	mmu-miR-598	mmu-miR-219-3p
129	mmu-miR-146a	mmu-miR-421
130	mmu-miR-219-3p	mmu-miR-140*
131	mmu-miR-532-5p	mmu-miR-874
132	mmu-miR-874	mmu-miR-664
133	mmu-miR-361	mmu-miR-137
134	mmu-miR-137	mmu-miR-667
135	mmu-miR-29b	mmu-miR-128-1*
136	mmu-miR-667	mmu-miR-673-5p
137	mmu-miR-128-1*	mmu-miR-872*
138	mmu-miR-673-5p	mmu-miR-872*
	mmu-miR-872*	mmu-miR-676

139	mmu-miR-383	mmu-miR-320
140	mmu-miR-320	mmu-miR-384-3p
141	mmu-miR-671-3p	mmu-miR-370
142	mmu-miR-384-3p	mmu-miR-15a
143	mmu-miR-140*	mmu-miR-671-3p
144	mmu-miR-664	mmu-miR-411*
145	mmu-miR-676	mmu-miR-666-5p
146	mmu-miR-369-3p	mmu-miR-326
147	mmu-miR-335-5p	mmu-miR-127*
148	mmu-miR-127*	mmu-miR-369-3p
149	mmu-miR-298	mmu-miR-335-5p
150	mmu-miR-666-5p	mmu-miR-383
151	mmu-miR-485	mmu-miR-330*
152	mmu-miR-379	mmu-miR-351
153	mmu-miR-10a	mmu-miR-485
154	mmu-miR-3071*	mmu-miR-423-5p
155	mmu-miR-382	mmu-miR-27a
156	mmu-miR-330*	mmu-miR-382
157	mmu-miR-351	mmu-miR-652
158	mmu-miR-423-5p	mmu-miR-10a
159	mmu-miR-666-3p	mmu-miR-298
160	mmu-miR-708	mmu-miR-495
161	mmu-miR-495	mmu-let-7b*
162	mmu-let-7b*	mmu-miR-708
163	mmu-miR-93	mmu-miR-379
164	mmu-miR-27a	mmu-miR-3071*
165	mmu-miR-423-3p	mmu-miR-93
166	mmu-miR-125b-1-3p	mmu-miR-501-3p
167	mmu-let-7c-2*	mmu-miR-409-5p
168	mmu-let-7a-1*	mmu-miR-125b-1-3p
169	mmu-miR-652	3p
170	mmu-miR-3475	mmu-miR-24-2*
171	mmu-miR-135a	mmu-miR-423-3p
172	mmu-miR-873	mmu-miR-666-3p
173	mmu-miR-329*	mmu-miR-331-3p
174	mmu-miR-31	mmu-miR-451
175	mmu-miR-409-5p	mmu-miR-3059
176	mmu-miR-154	mmu-miR-3475
177	mmu-miR-501-3p	mmu-miR-31
178	mmu-miR-323-3p	mmu-miR-329*
179	mmu-miR-3059	mmu-let-7c-2*
180	mmu-miR-24-2*	mmu-let-7a-1*
181	mmu-miR-194	mmu-miR-187
182	mmu-miR-326	mmu-miR-3068*
183	mmu-miR-145	mmu-miR-145
184	mmu-miR-451	mmu-miR-323-3p
185	mmu-miR-3068*	mmu-miR-194
186	mmu-miR-338-5p	mmu-miR-135a
187	mmu-miR-379*	mmu-miR-154
		mmu-miR-344

188	mmu-miR-7a	mmu-miR-873
189	mmu-miR-1198-5p	mmu-miR-1198-5p
190	mmu-miR-142-5p	mmu-miR-338-5p
191	mmu-miR-376a*	mmu-miR-379*
192	mmu-miR-187	mmu-miR-376a*
193	mmu-miR-331-3p	mmu-miR-344b
194	mmu-miR-1298*	mmu-miR-142-5p
195	mmu-miR-375	mmu-miR-375
196	mmu-miR-322	mmu-miR-361*
197	mmu-miR-1298	mmu-miR-322
198	mmu-miR-361*	mmu-miR-488*
199	mmu-miR-344	mmu-miR-1298*
200	mmu-miR-551b	mmu-miR-185
201	mmu-miR-431*	mmu-miR-203
202	mmu-miR-344b	mmu-miR-431*
		mmu-miR-129-1-
203	mmu-miR-673-3p	3p
204	mmu-miR-185	mmu-miR-676*
205	mmu-miR-30d*	mmu-miR-30d*
206	mmu-miR-429	mmu-miR-324-5p
207	mmu-miR-676*	mmu-miR-7a
208	mmu-miR-221*	mmu-miR-673-3p
209	mmu-miR-28	mmu-miR-28
210	mmu-miR-488*	mmu-miR-199a-3p
211	mmu-miR-873*	mmu-miR-199b
212	mmu-miR-543	mmu-miR-1298
213	mmu-miR-129-1-3p	mmu-miR-221*
214	mmu-miR-324-5p	mmu-miR-5117
215	mmu-miR-490-3p	mmu-miR-152
216	mmu-miR-5117	mmu-miR-543
217	mmu-miR-592	mmu-let-7f-2*
218	mmu-miR-376b	mmu-miR-551b
219	mmu-miR-346	mmu-miR-346
220	mmu-let-7f-2*	mmu-miR-133a
221	mmu-miR-34a	mmu-miR-3102
222	mmu-miR-3102	mmu-miR-490-3p
223	mmu-miR-431	mmu-miR-30c-2*
224	mmu-miR-329	mmu-miR-873*
225	mmu-miR-376a	mmu-miR-329
226	mmu-miR-133a	mmu-miR-592
227	mmu-miR-340-3p	mmu-miR-429
228	mmu-let-7e*	mmu-let-7e*
229	mmu-miR-485*	mmu-miR-3085-3p
230	mmu-miR-30c-2*	mmu-miR-30c-1*
231	mmu-miR-152	mmu-miR-431
232	mmu-miR-134	mmu-miR-345-5p
233	mmu-miR-30c-1*	mmu-miR-376b
234	mmu-miR-199a-3p	mmu-miR-1839-3p
235	mmu-miR-199b	mmu-miR-485*
236	mmu-miR-203	mmu-miR-340-3p

237	mmu-miR-674*	mmu-miR-674*
238	mmu-miR-200b	mmu-miR-134
239	mmu-miR-582-5p	mmu-miR-148a*
240	mmu-miR-19b	mmu-miR-1981*
241	mmu-miR-3085-3p	mmu-miR-34a
242	mmu-miR-7a-1*	mmu-miR-19b
243	mmu-miR-1981*	mmu-miR-582-5p
244	mmu-miR-182	mmu-miR-7a-1*
245	mmu-miR-148a*	mmu-miR-877*
246	mmu-miR-7b	mmu-miR-10b
247	mmu-miR-674	mmu-miR-702
248	mmu-miR-877*	mmu-miR-193b
249	mmu-miR-1839-3p	mmu-miR-365
250	mmu-miR-98*	mmu-miR-124*
251	mmu-miR-99a*	mmu-miR-148b*
252	mmu-miR-190	mmu-miR-98*
253	mmu-miR-124*	mmu-miR-190
254	mmu-miR-433*	mmu-miR-376a
255	mmu-miR-148b*	mmu-miR-99a*
256	mmu-miR-3102-3p.2	mmu-miR-664*
257	mmu-miR-702	mmu-miR-210
258	mmu-miR-2182	mmu-miR-674
259	mmu-miR-27b*	mmu-miR-200b
260	mmu-miR-29a*	mmu-miR-3102-3p.2
261	mmu-miR-365	mmu-miR-27b*
262	mmu-miR-140	mmu-miR-7b
263	mmu-miR-874*	mmu-miR-874*
264	mmu-miR-3099	mmu-miR-140
265	mmu-miR-1224	mmu-miR-133b
266	mmu-miR-200a	mmu-miR-182
267	mmu-miR-193b	mmu-miR-770-5p
268	mmu-miR-345-5p	mmu-miR-433*
269	mmu-miR-133b	mmu-miR-2182
270	mmu-miR-744*	mmu-miR-29a*
271	mmu-miR-3078	mmu-miR-22*
272	mmu-miR-210	mmu-miR-3099
273	mmu-miR-664*	mmu-miR-1224
274	mmu-miR-1247	mmu-miR-106b
275	mmu-miR-106b	mmu-miR-744*
276	mmu-miR-101a*	mmu-miR-7a-2*
277	mmu-miR-770-5p	mmu-miR-145*
278	mmu-miR-7a-2*	mmu-miR-677
279	mmu-miR-22*	mmu-miR-770-3p
280	mmu-miR-770-3p	mmu-miR-101a*
281	mmu-miR-145*	mmu-miR-3078
282	mmu-miR-376c	mmu-miR-99b*
283	mmu-miR-377*	mmu-miR-191*
284	mmu-miR-191*	mmu-miR-377*
285	mmu-miR-219-5p	mmu-miR-672

286	mmu-miR-677	mmu-miR-28*
287	mmu-miR-130b	mmu-miR-1247
288	mmu-miR-672	mmu-miR-376c
289	mmu-miR-425*	mmu-miR-17
290	mmu-miR-17	mmu-miR-130b
291	mmu-miR-671-5p	mmu-miR-200a
292	mmu-miR-28*	mmu-miR-532-3p
293	mmu-miR-342-5p	mmu-miR-3082-3p
294	mmu-miR-99b*	mmu-miR-1843-3p
295	mmu-miR-15b	mmu-miR-152*
296	mmu-miR-532-3p	mmu-miR-425*
297	mmu-miR-325	mmu-miR-374
298	mmu-miR-296-5p	mmu-let-7i*
299	mmu-miR-3082-3p	mmu-miR-342-5p
300	mmu-miR-10b	mmu-miR-29c*
301	mmu-miR-700*	mmu-miR-195*
302	mmu-miR-764-3p	mmu-miR-15b
303	mmu-miR-20a	mmu-miR-339-3p
304	mmu-miR-574-3p	mmu-miR-700*
305	mmu-miR-195*	mmu-miR-1983
306	mmu-miR-374	mmu-miR-455
307	mmu-miR-1843-3p	mmu-let-7f-1*
308	mmu-miR-222*	mmu-miR-296-5p
309	mmu-miR-29c*	mmu-miR-671-5p
310	mmu-miR-301b	mmu-miR-500
311	mmu-miR-500	mmu-miR-574-3p
312	mmu-miR-3093-5p	mmu-miR-301b
313	mmu-miR-34b-3p	mmu-miR-222*
314	mmu-miR-1983	mmu-miR-3057-5p
315	mmu-let-7g*	mmu-miR-3093-5p
316	mmu-miR-138-1*	mmu-miR-378*
317	mmu-miR-1981	mmu-miR-325
318	mmu-miR-3061-3p	mmu-miR-3061-3p
319	mmu-let-7f-1*	mmu-miR-322*
320	mmu-miR-34b-5p	mmu-miR-20a
321	mmu-miR-130b*	mmu-miR-3084
322	mmu-miR-322*	mmu-miR-1981
323	mmu-let-7i*	mmu-let-7g*
324	mmu-miR-299*	mmu-miR-106b*
325	mmu-miR-106b*	mmu-miR-1224*
326	mmu-miR-339-3p	mmu-miR-138-1*
327	mmu-miR-1224*	mmu-miR-130b*
328	mmu-miR-378*	mmu-miR-3068
329	mmu-miR-344d-3*	mmu-miR-219-5p
330	mmu-miR-3068	mmu-miR-125a-3p
331	mmu-miR-496	mmu-miR-299*
332	mmu-miR-218-2*	mmu-miR-764-3p
333	mmu-miR-3084	mmu-miR-24-1*
334	mmu-miR-152*	mmu-miR-34b-3p
335	mmu-miR-135b	mmu-miR-337-3p

336	mmu-miR-125a-3p	mmu-miR-218-2*
337	mmu-miR-337-3p	mmu-miR-128-2*
338	mmu-miR-299	mmu-miR-299
339	mmu-miR-3057-5p	mmu-miR-496
340	mmu-miR-128-2*	mmu-miR-26b*
341	mmu-miR-26b*	mmu-miR-344c
342	mmu-miR-543*	mmu-miR-144*
343	mmu-miR-879*	mmu-miR-1947
344	mmu-miR-377	mmu-miR-879*
345	mmu-miR-144*	mmu-miR-344d-3*
346	mmu-miR-24-1*	mmu-miR-3083
347	mmu-miR-3083	mmu-miR-339-5p
348	mmu-miR-344c	mmu-miR-350
349	mmu-miR-350	mmu-miR-504
350	mmu-miR-218-1*	mmu-miR-188-5p
351	mmu-miR-135a-2*	mmu-miR-377
352	mmu-miR-188-5p	mmu-miR-3096b-5p
353	mmu-miR-455	mmu-miR-138-2*
354	mmu-miR-339-5p	mmu-miR-323-5p
355	mmu-miR-323-5p	mmu-miR-543*
356	mmu-miR-138-2*	mmu-miR-30b*
357	mmu-miR-30b*	mmu-miR-218-1*
358	mmu-miR-183	mmu-miR-135a-2*
359	mmu-miR-504	mmu-miR-34b-5p
360	mmu-miR-1947	mmu-miR-210*
361	mmu-miR-21*	mmu-miR-539-5p
362	mmu-miR-3096b-5p	mmu-miR-135b
363	mmu-miR-139-3p	mmu-miR-139-3p
364	mmu-miR-539-5p	mmu-miR-183
365	mmu-miR-210*	mmu-miR-21*
366	mmu-miR-679-5p	mmu-miR-184
367	mmu-miR-184	mmu-miR-486*
368	mmu-miR-1264-3p	mmu-miR-455*
369	mmu-miR-3087	mmu-miR-380-5p
370	mmu-miR-93*	mmu-miR-362-3p
371	mmu-miR-455*	mmu-miR-345-3p
372	mmu-miR-34c*	mmu-let-7c-1*
373	mmu-miR-325*	mmu-miR-3060
374	mmu-miR-380-5p	mmu-miR-199a-5p
375	mmu-miR-362-3p	mmu-miR-93*
376	mmu-miR-450b-5p	mmu-miR-1943
377	mmu-let-7c-1*	mmu-miR-142-3p
378	mmu-miR-1943	mmu-miR-325*
379	mmu-miR-193	mmu-miR-679-5p
380	mmu-miR-3060	mmu-miR-450b-5p
381	mmu-miR-33	mmu-miR-193
382	mmu-miR-3072	mmu-miR-3087
383	mmu-miR-450a	mmu-miR-467a
384	mmu-miR-345-3p	mmu-miR-26a-2*

385	mmu-miR-669c	mmu-miR-3072
386	mmu-miR-491	mmu-miR-1264-3p
387	mmu-miR-142-3p	mmu-miR-34c*
388	mmu-miR-700	mmu-miR-700
389	mmu-miR-448-3p	mmu-miR-448-3p
390	mmu-miR-486*	mmu-miR-1964-3p
391	mmu-miR-300*	mmu-miR-491
392	mmu-miR-1964-3p	mmu-miR-7b*
393	mmu-miR-544-3p	mmu-miR-450a
394	mmu-miR-467a	mmu-miR-669c
395	mmu-miR-185*	mmu-miR-215
396	mmu-miR-32	mmu-miR-32
397	mmu-miR-26a-2*	mmu-miR-33
398	mmu-miR-412-5p	mmu-miR-412-5p
399	mmu-miR-582-3p	mmu-miR-300*
400	mmu-miR-7b*	mmu-miR-185*
401	mmu-miR-542-3p	mmu-miR-3061-5p
402	mmu-miR-33*	mmu-miR-544-3p
403	mmu-miR-154*	mmu-miR-1982.1
404	mmu-miR-667*	mmu-miR-542-3p
405	mmu-miR-3061-5p	mmu-miR-582-3p
406	mmu-miR-1982.1	mmu-miR-3074-5p
407	mmu-miR-199a-5p	mmu-miR-31*
408	mmu-miR-540-5p	mmu-miR-219-3p*
409	mmu-miR-3069-3p	mmu-miR-33*
410	mmu-miR-215	mmu-miR-154*
411	mmu-miR-17*	mmu-miR-667*
412	mmu-miR-3074-5p	mmu-miR-540-5p
413	mmu-miR-1197	mmu-miR-3069-5p
414	mmu-miR-296-3p	mmu-miR-331-5p
415	mmu-miR-1193-3p	mmu-miR-1193-3p
416	mmu-miR-107*	mmu-miR-3069-3p
417	mmu-miR-19a	mmu-miR-17*
418	mmu-miR-219-3p*	mmu-miR-211
419	mmu-miR-92a-1*	mmu-miR-1197
420	mmu-miR-211	mmu-miR-92a-1*
421	mmu-miR-539-3p	mmu-let-7a-2*
422	mmu-miR-1a	mmu-miR-29b-1*
423	mmu-miR-337-5p	mmu-miR-3074-1-3p
424	mmu-miR-29b-1*	mmu-miR-19a
425	mmu-miR-362-5p	mmu-miR-449a
426	mmu-miR-29b-2*	mmu-miR-362-5p
427	mmu-miR-3074-1-3p	mmu-miR-141
428	mmu-miR-1b-5p	mmu-miR-1a
429	mmu-miR-551b*	mmu-miR-187*
430	mmu-miR-544-5p	mmu-miR-296-3p
431	mmu-miR-155	mmu-miR-27a*
432	mmu-miR-494	mmu-miR-1b-5p
433	mmu-miR-672*	mmu-miR-107*

434	mmu-miR-467e	mmu-miR-3093-3p
435	mmu-miR-3069-5p	mmu-miR-491*
436	mmu-miR-31*	mmu-miR-186*
437	mmu-miR-100*	mmu-miR-155
438	mmu-miR-188-3p	mmu-miR-467e
439	mmu-miR-505-3p	mmu-miR-670*
440	mmu-miR-331-5p	mmu-miR-337-5p
441	mmu-miR-449a	mmu-miR-208b
442	mmu-miR-186*	mmu-miR-16-1*
443	mmu-miR-190*	mmu-miR-672*
444	mmu-let-7a-2*	mmu-miR-100*
445	mmu-miR-92b*	mmu-miR-3077
446	mmu-miR-467d	mmu-miR-381*
447	mmu-miR-3093-3p	mmu-miR-551b*
448	mmu-miR-3077	mmu-miR-505-3p
449	mmu-miR-669a-3p	mmu-miR-92b*
450	mmu-miR-669o-3p	mmu-miR-669a-3p
451	mmu-miR-1948	mmu-miR-669o-3p
452	mmu-miR-505-5p	mmu-miR-3084*
453	mmu-miR-15b*	mmu-miR-505-5p
454	mmu-miR-3071	mmu-miR-544-5p
455	mmu-miR-381*	mmu-miR-494
456	mmu-miR-27a*	mmu-miR-1948
457	mmu-miR-25*	mmu-miR-1982.2
458	mmu-miR-137*	mmu-miR-190*
459	mmu-miR-448-5p	mmu-miR-188-3p
460	mmu-miR-3084*	mmu-miR-690
461	mmu-miR-466p-3p	mmu-miR-143*
462	mmu-miR-466b-3p	mmu-miR-137*
463	mmu-miR-466c-3p	mmu-miR-1251
464	mmu-miR-187*	mmu-miR-539-3p
465	mmu-miR-670*	mmu-miR-190b
466	mmu-miR-190b	mmu-miR-15b*
467	mmu-miR-141	mmu-miR-467d
468	mmu-miR-690	mmu-miR-223
469	mmu-miR-1251	mmu-miR-29b-2*
470	mmu-miR-3572	mmu-miR-3071
471	mmu-miR-208b	mmu-miR-3572
472	mmu-miR-16-1*	mmu-miR-3103
473	mmu-miR-466a-3p	mmu-miR-421*
474	mmu-miR-466e-3p	mmu-miR-487b*
475	mmu-miR-574-5p	mmu-miR-204*
476	mmu-miR-1982.2	mmu-miR-25*
477	mmu-miR-223	mmu-miR-26a-1*
478	mmu-miR-150*	mmu-miR-344f-3p
479	mmu-miR-421*	mmu-miR-466p-3p
480	mmu-miR-1264-5p	mmu-miR-466b-3p
481	mmu-miR-487b*	mmu-miR-466c-3p
482	mmu-miR-3076-3p	mmu-miR-3102-5p.2

483	mmu-miR-499	mmu-miR-18a*
484	mmu-miR-143*	mmu-miR-150*
485	mmu-miR-18a*	mmu-miR-410*
486	mmu-miR-344f-3p	mmu-miR-466a-3p
487	mmu-miR-18a	mmu-miR-466e-3p
488	mmu-miR-26a-1*	mmu-miR-448-5p
489	mmu-miR-3102-5p.2	mmu-miR-1264-5p
490	mmu-miR-3103	mmu-miR-301a*
491	mmu-miR-410*	mmu-miR-3076-3p
492	mmu-miR-301a*	mmu-miR-574-5p
493	mmu-miR-495*	mmu-miR-499
494	mmu-miR-491*	mmu-miR-495*
495	mmu-miR-204*	mmu-miR-18a

Table S5: Primers used in the study

Name	Target	Forward primer (5'->3')	Reverse primer (5'->3')
<i>Kat2a</i>	mRNA	GAAGAGGGACCCCTCATCCTCA	GGAGAATTGCCCCGTAGAT
<i>Htr1a</i>	mRNA	CCCCTTCAGCTGTATCTTCC	AAAATGCAGCACGGGTTT
<i>Htr1b</i>	mRNA	GTCCTGCTGGTTGCTTGTT	TCCGATACACCGTAGCGATT
<i>Htr2a</i>	mRNA	CTGCTGGGTTTCCCTGTCAT	GTAAATCCAGACGGCACAGAG
<i>Htr2c</i>	mRNA	TGCTTAAAAGTGAAGCAATAATGG	AGGCCAATTAGGTGCACAAG
<i>Hcrtr2</i>	mRNA	GCTCACCAAGCATAAGCACAC	GGTACTCCCTGCTGTAGATACCA
<i>Penk</i>	mRNA	CCCAGGCGACATCAATT	TCTCCCAGATTTGAAAGAAGG
<i>Npbwr1</i>	mRNA	TCGTCTACGGGTAATTGC	GTACGTACAGCACCGCAGAG
<i>Hprt</i>	mRNA Reference	TCCTCCTCAGACCGCTTT	CCTGGTTCATCATCGCTAAC
<i>Hcrtr2</i> promoter	ChIP DNA, predicted NFkB- binding site	GCTCTTAGGCAGCTTCTCC	CAATGCCTCCAGAGCCTTG
<i>Npbwr1</i> promoter	ChIP DNA, predicted NFkB- binding site	TTCCTCCCTGACCTCCCC	TTACCTGGCGAGTCCCAGC

Table S6 Edited variant frequency of Htr2c mRNA.

Comparison to published dataset using 454 pyrosequencing (significant changes in *Kat2a* cKO mice are marked in bold, increased:red; decreased:blue)

Rank	Average relative occurrence in control CA1	Edited sites / Isoform	Sequence of edited cassette as seen in RNA-seq data	Edited protein sequence	Average relative occurrence in hypothalamus (Schellekens et al.,2012)
1	41.51%	ABD	GTGCGTAATCCTG	VNV	33.58%
2	10.60%	ABCD	GTGCGTAGTCCTG	VSV	11.32%
3	10.50%	AB	GTGCGTAATCCTA	VNI	19.31%
4	8.25%	(unedited)	ATACGTAATCCTA	INI	6.24%
5	7.19%	A	GTACGTAATCCTA	VNI	8.68%
6	5.63%	ABC	GTGCGTAGTCCTA	VSI	8.82%
7	4.44%	D	ATACGTAATCCTG	INV	2.66%
8	2.10%	AD	GTACGTAATCCTG	VNV	<1%
9	1.49%	AC	GTACGTAGTCCTA	VSI	1.11%
10	1.23%	ACD	GTACGTAGTCCTG	VSV	<1%
11	<1%	AE	GTACGTGATCCTA	VDI	<1%
11	<1%	C	ATACGTTAGTCCTA	ISI	<1%
11	<1%	DE	ATACGTGATCCTG	IDV	<1%
11	<1%	ABCDE	GTGCGTGGTCCTG	VGV	<1%
11	<1%	ABCE	GTGCGTGGTCCTA	VDV	<1%
11	<1%	ABDE	GTGCGTGATCCTG	VDV	<1%
11	<1%	ABE	GTGCGTGATCCTA	VDI	<1%
11	<1%	ACDE	GTGCGTGGTCCTA	VGV	<1%
11	<1%	ACE	GTACGTGGTCCTA	VGI	<1%
11	<1%	ADE	GTACGTGATCCTG	VDV	<1%
11	<1%	B	ATGCGTAATCCTA	MNI	<1%
11	<1%	BC	ATGCGTAGTCCTA	MSI	<1%
11	<1%	BCD	ATGCGTAGTCCTG	MSV	<1%
11	<1%	BCDE	ATGCGTGGTCCTG	MGV	<1%
11	<1%	BD	ATGCGTAATCCTG	MNV	<1%
11	<1%	BDE	ATGCGTGATCCTG	MDV	<1%
11	<1%	BE	ATGCGTGATCCTA	MDI	<1%
11	<1%	BCE	ATGCGTGGTCCTA	MGI	<1%
11	<1%	CD	ATACGTTAGTCCTG	ISV	<1%
11	<1%	CDE	ATACGTGGTCCTG	IGV	<1%
11	<1%	CE	ATACGTGGTCCTA	IGI	<1%
11	<1%	E	ATACGTGATCCTA	IDI	<1%