

## Supplemental Methods and References

### 1) Generation of *Tet1<sup>Δe4/-</sup>* ESCs

We generated homozygous *Tet1<sup>Δe4/-</sup>* ESCs through sequential targeting with our *Tet1* construct (**Fig. S1D**). Briefly, heterozygous *Tet1<sup>e4/+f</sup>* ESCs were electroporated with a Flp plasmid containing puromycin resistance. Colonies were picked, expanded, and split in order to perform selection with puromycin and neomycin in parallel. We confirmed excision of the neo cassette by PCR in those clones that survived puromycin selection but were susceptible to neomycin. Neo(-) cells were electroporated with the original construct again to generate homozygous *Tet1<sup>e4/f/f</sup>* ESCs. After selection with neomycin, homozygous *Tet1<sup>e4/f/f</sup>* ESCs were identified by Southern blot using both a 5' and 3' probe. Homozygous *Tet1<sup>e4/f/f</sup>* ESCs were then electroporated with a Cre plasmid containing puromycin resistance. After selection with puromycin, we identified *Tet1<sup>Δe4/-</sup>* ESCs by PCR confirmation of deleted exon 4.

### 2) PCR genotyping

DNA and cDNA genotyping for *Tet1* mutant mice was routinely done by PCR using the primers listed in **Supplemental Methods**. The DNA primers of GF1 and GR1 are for wild-type (217bp) and floxed (304bp), and GF2 and GR1 are for exon4 deletion (151bp). The cDNA primers CF1 and CR1 are for wild-type (246 bp), and CF2 and CR1 are for exon4 deletion (182 bp).

### 3) Preparation of nuclear protein and immunoblot analysis

Hippocampal tissue from the brains of *Tet1<sup>Δe4</sup>* mice were homogenized in HEPES-buffered sucrose (0.32 M sucrose, 4 mM HEPES, pH 7.4) and centrifuged at 800 × g for 10 min at 4°C. The pellet including nuclear proteins was washed one time with 1 × PBS and then centrifuged at 2000 × g for 10 min at 4°C. The washed pellet was dissolved in RIPA buffer and protein concentration was measured by a BCA kit (ThermoFisher

Scientific, Grand Island, NY). Equal amount of protein was separated by SDS-PAGE and then transferred to PVDF membranes (Bio-Rad, Hercules, CA). After blocking the membrane at room temperature for 1 hr in TRIS-buffered saline (pH 7.4, TBS) with 5% non-fat milk, the blots were incubated with anti-Tet1 antibody (GTX125888, GeneTex, Irvine, CA) and anti- $\beta$ -tubulin III antibody (ab18207, Abcam, Cambridge, MA) at 4°C overnight. The blots were washed in TBS containing 0.1% Tween-20 (TBST) and incubated with HRP-conjugated secondary antibodies for 60 min at room temperature. Following 3 washes in TBST, the blots were incubated with ECL reagent (GE Healthcare Life Sciences, Piscataway, NJ) and exposed to Kodak X-ray film (Rochester, NY).

#### **4) RNA isolation, qRT-PCR, & 5' Rapid Amplification of cDNA Ends (RACE)**

RNA from tissue or ESCs was isolated using SV Total RNA Isolation System (Promega) with DNase treatment. cDNA was prepared from 2ug of total RNA using Superscript III Reverse Transcriptase and oligo(dT) primer (ThermoFisher). cDNA was quantified by using SsoAdvanced Universal SYBR Green (Bio-rad) on a LightCycler 480 II (Roche) with a 10s denaturing step at 95°C and 20s annealing step at 59°C for 40 cycles. All qPCR results were normalized to *Gapdh*. *Oxtr* isoform qRT-PCR results were confirmed by using random primers to generate cDNA in a second round of testing. 5' RACE products were generated from RNA using the 5'/3' RACE kit, 2<sup>nd</sup> generation (Roche). 5' RACE products were gel separated, excised, cloned, and sequenced. All primers used are listed in below

#### **5) hMeDIP & qPCR**

DNA from mouse hippocampus was isolated using DNeasy Blood & Tissue Kit (Qiagen). DNA containing 5-hydroxymethylcytosine was immunoprecipitated using the hMeDIP Kit from Active Motif (cat. no. 55010). Briefly, DNA was fragmented to 200-600bp in size using an ultrasonic processor (Ultrasonics). Double-stranded DNA was then incubated overnight with 5-hydroxymethylcytidine pAb (13488) or Rabbit IgG control Ab (103524) and pulled down with magnetic beads. DNA was then further purified using Chromatin IP DNA Purification Kit (Active Motif) before analysis by qPCR. qPCR was performed using primers specific for the BS3 region using iTaq Universal SYBR Green (Bio-Rad) on a LightCycler 480 II (Roche) with a 10s denaturing step at

95°C and 30s annealing/extension step at 60°C for 50 cycles. APC spike in control and primers were used as directed by kit.

#### A list of primer pairs used in this study

<u>Sequence (5'-3')</u>	<u>Primer Name</u>	<u>Experiment</u>	<u>Annealing Temp. (C°)</u>
TGTTGAGAAAAACGGCACTG	GF1	DNA Genotyping	59
TCGACTAGAGCTTGCAGAAC	GF2	DNA Genotyping	59
GATAGACCACGTGCCTGGAT	GR1	DNA Genotyping	59
GCATCAATCCTCAGGAAAGG	CF1	cDNA Genotyping	59
TGCACCTACTGCAAGAACG	CF2	cDNA Genotyping	59
TGGGCCTTTCTTTTG	CR1	cDNA Genotyping	59
TCCTGCTGTGGAAAGGTATC	Tet1_F	qRT-PCR	59
ACAGGTGCAGGTACGCTTT	Tet1_R	qRT-PCR	59
AAGGTGCCTCTGGAGTGTTG	Tet2_F	qRT-PCR	59
ACCAAGAAAGCAGCTCGAAA	Tet2_R	qRT-PCR	59
ATGGCCCCACTACTGACCTT	Tet3_F	qRT-PCR	59
TACAATGGGTGCACTGTGGT	Tet3_R	qRT-PCR	59
CGCCATGCAATTCCACTATCAAATAA	Bdnf_Exon 4F	qRT-PCR	60
GCCTTCATGCAACCGAAGTA	Bdnf_Exon 1-6R	qRT-PCR	60
AGTTTCAGGAATTAAAGGAAGCTG	Homer1a_F	qRT-PCR	60
CATGATTGCTGAATTGAATGTGTA	Homer1a_R	qRT-PCR	60
CTGCATCTACACTCGCAAGG	Npas4_F	qRT-PCR	59
GCCACAATGTCTTCAAGCTCT	Npas4_R	qRT-PCR	59
CATGGCCTCCGTGTTCCCT	GAPDH_F	qRT-PCR	59
TGATGTCATCATACCTGGCAGGTT	GAPDH_R	qRT-PCR	59
TTCTTCGTGCAGATGTGGAG	Oxtr_ABEFG_F (black arrows)	qRT-PCR	59

TGTAGATCCATGGGTTGCAG	Oxtr_ABEFG_R (black arrows)	qRT-PCR	59
GTAAATTGGTAGAGGATTAAGTTTTTTTATTTTG	Npas4_ex_F <sup>b</sup>	Bisulfite-sequencing	58
TATCTCACACAAATCCAATACTAAAATATC	Npas4_ex_R <sup>b</sup>	Bisulfite-sequencing	58
TTTGTAAAGGGTTTAGATTATTTAATTATGTATTG	Npas4_in_F <sup>b</sup>	Bisulfite-sequencing	58
AACCCAAACTACTCACCTCCAAC	Npas4_in_R <sup>b</sup>	Bisulfite-sequencing	58
AGTTGAGTTTTTTAAAAAGATGTAAAG	Oxtr_BS1_F	Bisulfite-sequencing	53
ATTAACCCAAAATTACCTTACAC	Oxtr_BS1_R	Bisulfite-sequencing	53
GGGTATATTTTTGGGGTTTTTA	Oxtr_BS2_F	Bisulfite-sequencing	53
ACCATCCACTATAATACAACCTCCC	Oxtr_BS2_R	Bisulfite-sequencing	53
TGGAGATAAGTTGATATTATTGATT	Oxtr_BS3_F	Bisulfite-sequencing	53
CTTTTCATAAAACACCTAACATC	Oxtr_BS3_R	Bisulfite-sequencing	53
TGCTAATGCTCGTCTCTCCA	Oxtr_RACE_R1	5'RACE	59
GAGCAGAGCAGCAGAGGAAG	Oxtr_RACE_R2	5'RACE	59
TGTAGATCCATGGGTTGCAG	Oxtr_RACE_R3	5'RACE	59
GGGTGTACCGAGAGAGACTGA	Oxtr_A_F (blue arrows)	qRT-PCR	59
GGTGAECTCTCGGTGGTGA	Oxtr_A_R (blue arrows)	qRT-PCR	59
TTCTCCTGGTTGTTCAAGG	Oxtr_B_F (purple arrows)	qRT-PCR	59
CCGAGGTCCAACTCGATACT	Oxtr_B_R (purple arrows)	qRT-PCR	59
GCCGCCTGCTATGGTCTC	Oxtr_ABE_F (green arrows)	qRT-PCR	59
CATCTGCACGAAGAAGAAAGG	Oxtr_ABE_R (green arrows)	qRT-PCR	59
TGCATTTGAGTCCAGTCACC	Oxtr_H_F (yellow arrows)	qRT-PCR	59
GGCAATGATGAAGGCAGAAG	Oxtr_H_R (yellow arrows)	qRT-PCR	59
TTCATCATTGCCATGCTCTT	Oxtr_A-H_F (red arrows)	qRT-PCR	59
TGCTAATGCTCGTCTCTCCA	Oxtr_A-H_R (red arrows)	qRT-PCR	59
CCGCAGGCTAGGTAGGAGTT	Oxtr_5'UTR_F	ChIP-qPCR	60
AGTGGATGGCCTCAGAGATG	Oxtr_5'UTR_R	ChIP-qPCR	60
CACTCGCGCCTCTCTTT	Oxtr_Exon3_F	ChIP-qPCR	60
GCAAGTATTGACCAGACGACA	Oxtr_Exon3_R	ChIP-qPCR	60

GCATCACCCGGAGGAGAAAATCGG	GAPDH-F	ChIP-qPCR	60
GTCACGTGTCGCAGAGGAGC	GAPDH-R	ChIP-qPCR	60
TGGAGATAAGTTGATATTATTGATT	BS3_F	hMeDIP-qPCR	60
CTTTTTCATAAACACCTAAACATC	BS3_R	hMeDIP-qPCR	60

. <sup>b</sup>Npas4 bisulfite sequencing primers from (Rudenko et al., 2013).

## 6) Electroconvulsive stimulation

Electroconvulsive shock (ECS) was administered via alligator clamps applied bilaterally to the ears of the mouse using a stimulator (Digitimer) and waveform generator (Agilent Trueform 33500 series). The following optimized parameters were used to generate a tonic-clonic seizure: 100 Hz, 0.2-ms pulse width, 18 mA stimulation for 1.15 seconds. Seizures typically lasted less than 1 min and mice typically recovered in 30-90 seconds by self-righting. We treated sham mice by applying the clamps without administering the shock. Hippocampi from *Tet1*<sup>Δe4/-</sup> and *Tet1*<sup>+/+</sup> mice (ECS and sham) were harvested 1.5-2 hours after stimulation, a timeframe when activity-dependent genes are known to be upregulated.

## 7) RNA-seq

RNA was isolated using Trizol Reagent (ThermoFisher) from ECS-treated hippocampal tissue from 3 *Tet1*<sup>Δe4/-</sup> and 3 *Tet1*<sup>+/+</sup> mice and the RNA integrity numbers (RINs) were determined using the 2100 Agilent Bioanalyzer 6000 Pico assay. Total RNA was amplified using the Clontech SMARTer Ultra Low RNA Kit according to the manufacturer's instructions. Sequencing

libraries were then prepared using the TruSeq RNA Sample Preparation Kit (Illumina). RNA libraries sequenced using the Illumina HiSeq 2000 system (Illumina, San Diego, CA). The trim galore (v 0.3.1) was used to remove adapters and duplicates. We used TopHat (version 2.0.9) to align reads to mouse genome (mm10) and Cufflinks (version 2.1.1) to find differentially expressed genes with default parameters. Only genes that had a status of "OK" and FPKM>=1 in either WTs or KOs were used in subsequent

analyses (12,659 out of 23,360 genes). The list of significantly differentially expressed genes was defined at false discovery rate (FDR)<0.05. Gene Ontology analysis was performed using DAVID to investigate whether dysregulated genes were enriched in any particular category of genes.

A list of neuronal activity-dependent genes was generated by searching the literature and including genes that have been implicated in at least two independent studies (**Table S2**) (1-7). *Tet1<sup>Δe4/-</sup>* dysregulated genes were not significantly overlapped with known activity-dependent genes (number of overlap genes=11, Odds ratio=1.477801, *p*=0.1932, Fisher's exact test). Our set of dysregulated genes was compared to dysregulated genes reported in *Tet1* exon 5 deficient ( $\Delta e5$ ) hippocampus (8) *Tet1* exon 11-13 deletion ( $\Delta e11-13$ ) neural progenitor cells (9), *Tet1*-knockdown ESCs (10), and *Tet1* gene-trap primordial germ cells (11). Significant overlap was determined by Fisher's exact test in R (<http://www.r-project.org/>), 14,601 genes were used as background.

## **8) Targeted Bisulfite genome sequencing**

2ug DNA from each sample was bisulfite-converted using the EpiTect bisulfite kit (Qiagen, Valencia, CA, USA) according to the manufacturer's protocol. Bisulfite-converted DNA was amplified in 40 cycles using EpiMark Hot Start Taq DNA polymerase (NEB). Specific primers and annealing temperatures are listed in below. PCR fragments were recovered by gel excision and cloned into the pGEM-T easy vector (Promega, Madison, WI, USA). Typically, 16 clones from each PCR product were sequenced with M13R primers at Beckman Coulter Genomics (Danvers, MA, USA) or EtonBio (Research Triangle Park, NC, USA). A minimum of 10–12 clones with good quality of sequence was obtained for each sample. Sequencing reads were analyzed using the online platform BISMA (12) using default analysis parameters: Lower threshold conversion rate 95%, Lower threshold sequence identity 90%, Upper threshold of N-sites at cytosine position 20%, Upper threshold gaps allowed 20%.

## **9) Methylome production & analysis**

Whole genome bisulfite sequencing – 6ug DNA was mixed with 25ng lambda DNA and sonicated to 200-500bp. DNA was end-repaired, adenylated, and ligated to TrueSeq sequencing adaptors. DNA was purified by AMPure beads or DNA purification kit according to the DNA amount after each step. Library DNA was amplified by PfuTurbo Cx Hotstart DNA polymerase (Agilent, for bisulfite treated DNA libraries). 2% agarose gel was used to select 200-500bp DNA fragments after PCR amplification. Bisulfite treatment was performed using commercial kit (Zymo research, Cat. D5005). DNA was amplified and 200-500bp fragments were gel selected. MethylC-Seq was performed as previously described(13, 14). Briefly, extracted DNA (DNeasy Kit, Qiagen) was spiked with unmethylated lambda DNA (Promega) at 0.5%, sonicated (Bioruptor, Diagenode), end-repaired, adenylated, and ligated to Illumina TruSeq sequencing adapters. After 2% agarose gel purification to select fragments of size 200–650 bp, samples were subjected to bisulfite conversion (MethylCode, Invitrogen) and PCR amplification with PfuTurbo Cx Hotstart DNA Polymerase (Agilent). After gel purification, libraries were sequenced on an Illumina Hi-Seq 2000.

We obtained a total of 66,939,297 raw reads (100 bases per read) for *Tet1*<sup>+/+</sup> cerebral cortex tissue. Among them, 50,172,066 (87.1%) were mapped to the mouse genome mm9 reference assembly uniquely using BSMAP (27) with parameters -r 0 -w 100 -v 0.1, adaptor sequence was removed with parameter -A. The duplicated reads accounted for 12.9% were removed. For *Tet1*<sup>Δe4/-</sup> cerebral cortex tissue we have obtained a total of 53,752,766 raw reads (100 bases per read). Among them, 36,652,181 (89.7%) reads were mapped to the genome uniquely with duplicated reads occupying 11.3%. After removing duplicated reads, a total of 43,700,312 and 32,511,816 monoclonal reads for *Tet1*<sup>+/+</sup> and *Tet1*<sup>Δe4/-</sup>, respectively, were used for subsequently analysis. The bisulfite conversion rate is 99.44% and 99.41% for *Tet1*<sup>+/+</sup> and *Tet1*<sup>Δe4/-</sup>, respectively.

#### **Identification differential methylation regions (DMRs) in *Tet1* mutant mice**

For the analysis of identifying DMRs, a 200bp bin was chosen as a basic unit for analysis. Bins with a total CG coverage less than 5x were removed. A total of 2,997,308

and 2,163,498 bins that cover the 46.1% and 36.8% of total CpG sites for *Tet1*<sup>+/+</sup> and *Tet1*<sup>Δe4-/-</sup>, respectively, were used for the final analysis. Methylation ratio was calculated using methylated CG verses total CG for each bin. The number given for mCG change is the results of *Tet1*<sup>+/+</sup> mCG level minus *Tet1*<sup>Δe4-/-</sup> mCG level in each CpG island located within promoters or intragenic regions. The hypermethylated and hypomethylated bins in *Tet1*<sup>Δe4-/-</sup> tissues were selected with a FDR < 0.05. Fisher's exact test was used to discover altered mCG in each 200bp bins with a threshold of *p*-value <0.05.

### **Analysis the pattern of histone modifications in *Tet1* DMR regions**

Fisher test was used to discover hypermethylated CpG in TET1 KO cortex in each 200bp bins with a threshold of *p*-value <0.05. 2000bp windows containing at least 4 continuous hypermethylated DMRs (200bp) are selected out as broad DMRs for analysis. Random regions were derived from regions covered by our methylome data. The K4me3, K27me3 and K4me1 ChIP-seq signals from ENCODE dataset in cortex (16) are mapped to both broad DMRs and random regions for comparison. Random regions were chosen from regions also covered by our methylome data. The *p*-value for the enrichment of *Tet1*-DMRs in genome was also calculated using fisher's P-value is calculated by t-test.

**Motif analysis of DMRs in *Tet1*<sup>e4-/-</sup> mice:** Motif analysis of hypermethylated DMRs in TET1 KO cortex (200bp bin, with *p*-value < 0.05 using fisher's test) was used an analysis tool HOMER2(17). The software was download from online and the instruction for the analysis was followed (<http://homer.ucsd.edu/homer/motif/>).

### **10) Behavioral tests**

We employed a battery of behavioral tests on multiple cohorts of mice at the Duke Mouse Behavior and Neuroendocrine Core Facility according to protocols described below. All experimenters handling animals or scoring behavioral data were blinded to genotype throughout the studies. We did not control for the estrus cycle in any of the tests. Mice in all cohorts were housed on a 14-hr light/ 10-hr dark cycle with most

testing occurring during the light cycle, 4-5 mice per cage, and *ad libitum* access to food and water, unless otherwise specified.

**Neurophysiological Screen** - Mice were examined for general appearance, orientation to a moving object, reflexes, posture, and grip strength using methods previously described (18, 19).

**Open field** - Spontaneous activity in the open field was conducted over 1 hr in an automated Omnitech Digiscan apparatus (AccuScan Instruments, Columbus, OH). Accuscan software scored the total distance traveled, vertical activity (beam-breaks), and time spent in the center zone.

**Rotarod** - Balance and coordination were examined using a rotarod (Med-Associates) as described (18). On day 1 the rod accelerated from 4 to 40 rpm over 5 min, and mice were given 4 successive 5-min trials with an inter-trial interval of 30 min. Trials were terminated when the mouse fell from the rod or at 300 s. On day 2 the rod was maintained at a steady speed of 24 rpm, and 4 trials were conducted in the same manner as on day 1.

**Light-dark emergence** - Mice were placed into the darkened side (~2 lux) of a 2-chambered apparatus (Med-Associates, St. Albans, VT) and given 5 min to freely explore the darkened and lighted (~750 lux) chambers. Infrared diodes within the test chamber tracked the location and activity of the animal throughout testing. The scored behaviors comprised the latency to enter into the lighted chamber, activity (beam breaks) within each chamber, and the numbers of crossings between the lighted and darkened chambers.

**Resident-Intruder**- Mice were individually housed for 3 weeks in order to increase propensity for aggressive behaviors in both male and female mice (20, 21). Sex-matched, non-familiar C3H mice (Jackson Labs, Stock No. 000659) of the same age and approximate weight were used as intruders. The test was performed in the dark, 2-6 hr after onset of the dark cycle in the resident's home cage. The home cage with the test mice was placed in the test arena and allowed to acclimatize for 5 minutes before an intruder mouse was added to the cage. The mice were allowed to freely interact for 5 minutes before the intruder was removed. The behavioral ethogram was established at the Duke Mouse Behavioral and Neuroendocrine Core Facility (22); individual behaviors

were collapsed into six categories: mild social investigation, non-social behaviors, withdrawal/disengagement, stationary reactivity, threatening postures, and attacks. Only one animal engaged in fighting necessitating early termination of the experiment and another animal left the testing arena during the last minute of the test. For these two animals we adjusted the final interactions proportionally based on levels of interactions up until the moment the test was ended. All tests were filmed and interactions of the following categories: mild social investigation, non-social behaviors, withdrawal/disengagement, stationary reactivity, threatening postures, and attack were scored by an observer blinded to the genotype of the mice after reviewing the filmed tests. The following behavior: feinting, rushing, mounting, clawing, pushing/shoving, climb-grooming, tail rattling were considered threatening postures. The biting, chasing, lunging, wrestling, and attacking were considered or scored as aggression behaviors. Data were expressed either the duration or frequency of certain behavioral category and ANOVA was used for the statistical analysis.

**Virgin pup retrieval** – Maternal behavior can be induced in virgin female mice by repeated exposure to pups (23-26). Maternal behaviors were tested in the home cage of each virgin female. Cage mates were removed during testing. For three consecutive days, 3-5 day-old pups were gently placed in the corners of the cage. Pups were left with the test mice for 1 hour and the first and last 15 minutes were recorded. Only wild-type C57BL/6J pups were used in order to limit the effect of pups' behavior on the behavior of the test females. Retrieval times were calculated from the first 15 minutes of the test. Crouching time was calculated from the last 15minutes of the test. Aggressive behaviors scored included tail rattling and attacks on the pups during the first 15 minutes of Day 1.

**Novel object recognition** - Mice were examined for short- and long-term memory in this task as described (27, 28). Testing was conducted over 5 min in four phases; object training (train), short-term recall at 30 min (STM), and long-term recall at 24 hr (LTM). At training, mice were exposed to a pair of identical objects (2 x 2 x 3 cm in size) affixed with double-sided tape to the floor of a white Plexiglas arena (41 x 18 x 30 cm); these objects constituted the “familiar” objects for the tests. In the short- and long-term memory tests, one of the two familiar objects was replaced with a novel object with

similar dimensions to the former but with different colors, patterns, and shapes. All tests were filmed with digital cameras and the videos were analyzed with Noldus Ethovision XT 7 software that automatically tracked the location of each animal as well as the location and movement of the animal's head and nose during testing. From these data, the total numbers of contacts and durations of object contacts were measured. Orientation and time spent with objects was defined as the animal's head oriented towards the object with the nose positioned within 2 cm of the object. Recognition scores were calculated by subtracting the time spent with the familiar from the time spent with the novel object, and dividing this difference by the total time spent with both objects. Positive scores signified recognition of the novel object, negative scores indicated preferences for the familiar object, and scores approaching 'zero' denoted preference for neither object.

**Morris water maze** - Spatial learning and memory, and plasticity were examined in the Morris water maze as described (29). All training and testing were conducted under ~125 lux illumination in a 120 cm diameter stainless-steel pool filled with water, made opaque with white non-toxic poster paint (Crayola LLC, Easton, PA) and maintained at 24°C. The pool was divided into four quadrants; northeast (NE), northwest (NW), southeast (SE) and southwest (SW). Before testing, mice were handled for 10 min and then acclimated to standing in water for 1 min over 5 consecutive days. Mice were trained next to sit on the hidden platform (1 cm below the water's surface and 20 cm from the rim of the pool) in the NE quadrant for 20 s and then allowed to swim freely for 60 s before being returned to the platform for 15s. On the following day, water-maze testing began with testing divided into 2 phases: acquisition (days 1-6) with the hidden platform in the NE quadrant and reversal (days 7-12) with the platform in the SW quadrant. Each day the mice received 4 trials in pairs that were separated by 60 min. Release points were randomized across test-trials and test-days. On days 2, 4, 6, 8, 10, and 12, a single probe trial was given 1 hr after the 4 test-trials. For probe trials, the platform was removed from the water and the mice were released from the southern-most point on days 2, 4, and 6, and from the northern-most point on days 8, 10, and 12. Performance on all tests was scored by Ethovision XT 7 (Noldus) using a high-resolution camera suspended 180 cm above the center of the pool. Tracking profiles

were generated by Ethovision software and were used to measure swim time. Except for probe trials (60 s in duration), all trials ended when the animal reached the platform or after 60 s of swimming.

**Social transmission of food preference** - Mice were examined for their abilities to select a familiar over a non-familiar food source as described (27, 28). *Tet1<sup>Δe4</sup>* mice were housed in groups of 3-4 animals with a WT littermate selected as the demonstrator. Three days prior to testing, animals were placed on food restriction. On the first test day, two flavored diets were prepared by mixing 50 g of ground mouse chow (Lab Diet Formula 5001; Purina Mills Inc., Richmond, VA) with 50 ml of water flavored with banana or maple extract. The demonstrator mouse was introduced into the test arena (41 x 18 x 30 cm) with a single 4 cm bowl containing 10 g of one of the flavored diets. The choice of the banana or maple diet was randomized among demonstrator mice such that genotype and sex of the *Tet1<sup>Δe4</sup>* cage-mates would be equally represented for each diet. The demonstrator was allowed to consume the flavored diet for 30 min and was returned to its home cage. Interactions between the demonstrator and *Tet1<sup>Δe4</sup>* cage-mates were filmed for 20 min, at which time the demonstrator was removed and housed separately for the duration of the study. *Tet1<sup>Δe4</sup>* tester mice were first examined in a two-way choice test beginning 20 min (short-term memory) after demonstrator removal. Individual *Tet1<sup>Δe4</sup>* testers were placed into the center of the arena and were given 15 min of free access to two 4 cm test-bowls placed at opposite ends of the chamber. One bowl contained the familiar demonstrator diet and the other contained the second or novel diet. Following testing, mice were returned to the home cage without the demonstrator animal. Twenty-four hours later, tester mice were re-examined in the same test arena with the familiar demonstrator diet and another novel diet flavored butter extract. Behaviors were filmed and later analyzed with the Noldus Observer XT 7 by trained observers blinded to the genotype and sex of the mice. For the choice tests with the tester mice, the bowls were weighed before and after testing; spillage was recovered and noted. Preference for a diet was determined by calculating the amount of novel diet consumed minus the amount of demonstrator diet consumed divided by the total amount eaten. Positive scores indicated preference for

the familiar demonstrator diet, whereas negative scores denoted preferences for the novel or unfamiliar diet. Scores approaching zero indicated no preference for either diet.

**Fear conditioning** - Animals were tested for contextual and cued fear conditioning as described (30). Mice were conditioned and tested in Med-Associates fear conditioning chambers under ~100 lux illumination. On day 1, mice were placed in the chamber for 2 min, after which a 72-dB 12-kHz tone (conditioned stimulus, CS) was presented for 30 s, which terminated simultaneously with a 2 s 0.4-mA scrambled foot-shock (unconditioned stimulus, UCS), which was repeated two subsequent times with an inter-stimulus interval of 60 seconds. Mice were removed from the conditioning chamber to the home cage 30 s later. For context testing on day 2, animals were returned to the chamber in which they had been conditioned for 5 min in the absence of the CS and UCS. For cued testing on day 3, the dimensions, texture and shape of the conditioning chamber were modified. Mice were introduced into the chamber for 2 min, after which the CS was presented for 3 min. For all tests, behavior was videotaped and scored in an automated fashion by FreezeScan (Cleversys, Reston VA) for freezing.

**General Statistical Analyses** - The data were analyzed with SPSS 21 (SPSS Inc., Chicago, IL) or Microsoft Excel and expressed as means  $\pm$  SEM. Simple comparisons between *Tet1<sup>Δe4/-</sup>* and *Tet1<sup>+/+</sup>* mice without regards to sex were conducted with independent t-tests. When comparisons between genotypes were made for within-subject measurements across different phases of the same test (e.g., test days, locations within a test arena, or different intensities of stimuli), the data were analyzed with repeated measures ANOVA (RMANOVA). For RMANOVAs, a Bonferroni-correction for multiple comparisons was applied to post-hoc t tests. Statistical significance was defined as  $p < 0.05$ . Sample sizes were based on previous experience with similarly designed experiments.

### **Supplemental References for method**

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# **Supplemental Figure (1-9) and Table (1-3)**

## **Epigenetic Dysregulation of *Oxtr* in *Tet1* Deficient Mice-Implication for Neuropsychiatric Disorders**

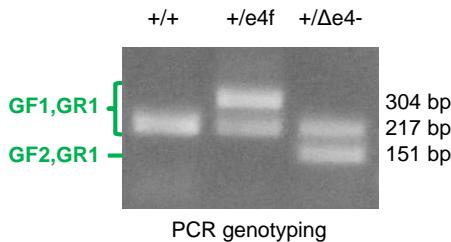
Aaron J Towers<sup>1#</sup>, Martine W Tremblay<sup>1#</sup>, Leeyup Chung<sup>2</sup>, Xin-lei Li<sup>2,7</sup>, Alexandra L Bey<sup>3</sup>,  
Wen-hao Zhang<sup>8</sup>, Xinyu Cao<sup>2</sup>, Xiaoming Wang<sup>2</sup>, Ping Wang<sup>2</sup>, Lara J Duffney<sup>2,3</sup>, Stephen K  
Siecinski<sup>1</sup>, Sonia Xu<sup>2</sup>, Yuna Kim<sup>2</sup>, Xiangyin Kong<sup>7</sup>, Simon Gregory<sup>1,4</sup>, Wei Xie<sup>7</sup>, Yong-hui Jiang<sup>1</sup>,  
2,3,5,6\*

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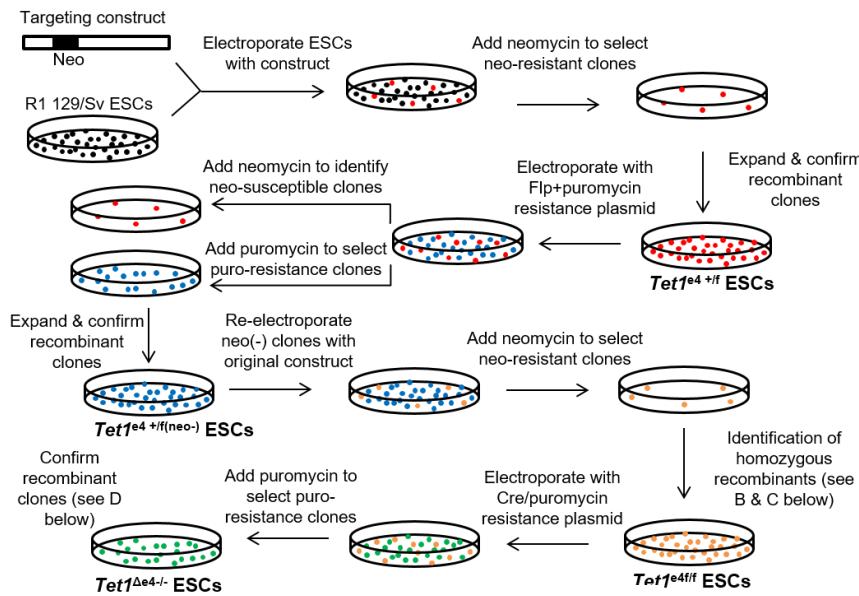
#Equal contribution

# Supplemental Figure 1

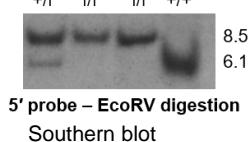
**A**



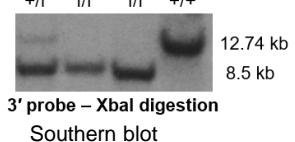
**B**



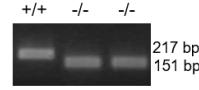
**C**



**D**



**E**



**Figure 1. Generation and Molecular Characterization of Tet1 Mutant (Tet1<sup>Δe4</sup>) ESCs & Mice**

- (A) PCR genotyping with the indicated primers (green) to confirm germline transmission of the Tet1<sup>e4f</sup> allele (+/e4f) and deletion of exon4 (+/Δe4-) after breeding with a CMV-Cre mouse. See the primer position in **Figure 1A**
- (B) A flow chart to generate homozygous Tet1<sup>Δe4/-</sup> ESCs through sequential targeting Tet1 ES cells
- (C-E) Molecular confirmation of homozygous Tet1<sup>Δe4/-</sup> ESCs. (C) DNA Southern blot confirmation of both alleles targeted ESCs after EcoRV digestion using the 5' probe (2nd & 3rd lanes). (D) DNA Southern blot confirmation of both alleles targeted ESCs after XbaI digestion using the 3' probe (2nd & 3rd lanes). (E) PCR genotyping confirmation of exon4 deletion (-/-) after electroporation with Cre plasmid.

## Supplemental Figure 2

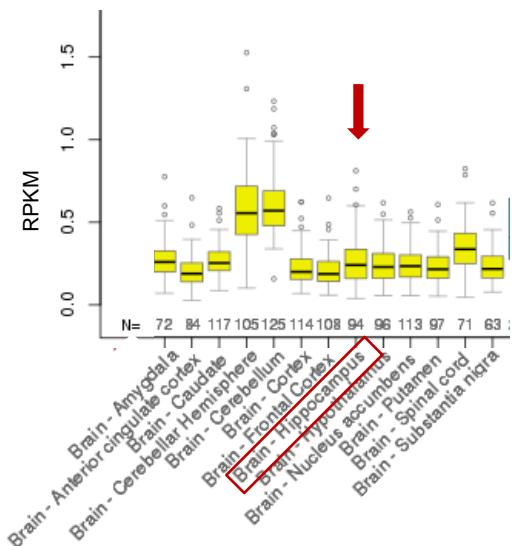
A



Tet1 expression in adult brain by RNA-in situ (Allen Brain Atlas)

B

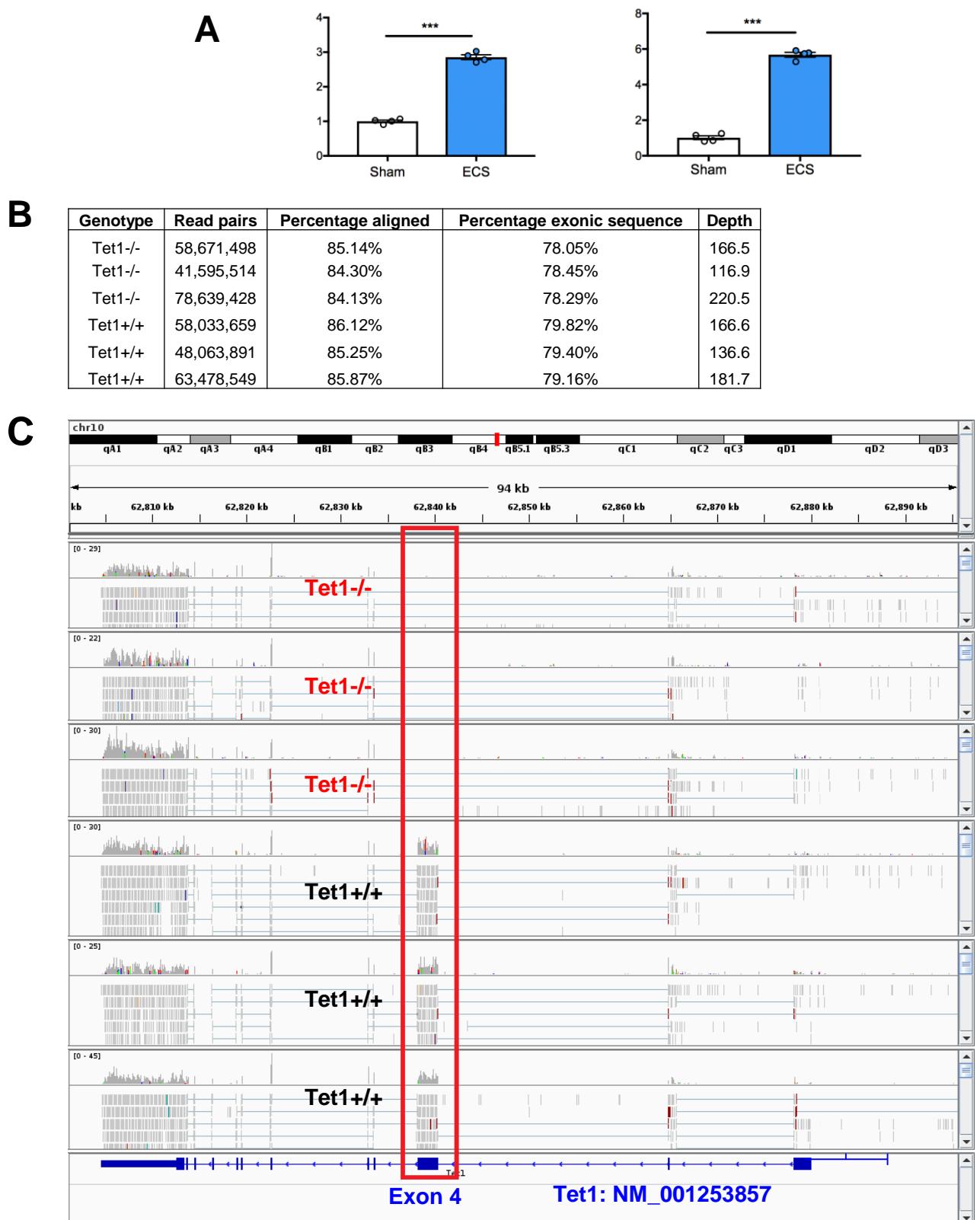
TET1 expression in brain by RNA-Seq Expression Data from GTEx (v6) in human genome browser: (genome.ucsc.edu)



**Figure. 2: Tet1 expression in mouse and human brain from in silico data**

- (A) The expression of Tet1 in adult mouse brain by RNA in situ (image from Allen Brain Atlas)
- (B) The expression of TET1 in human brains by RNA-seq experiments deposited in genome browser.

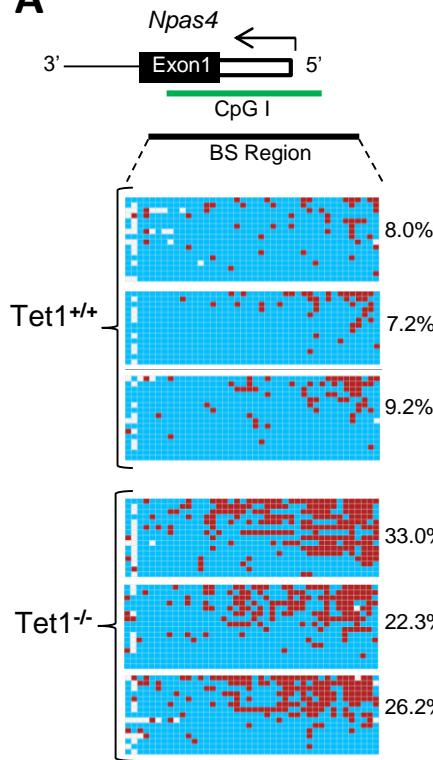
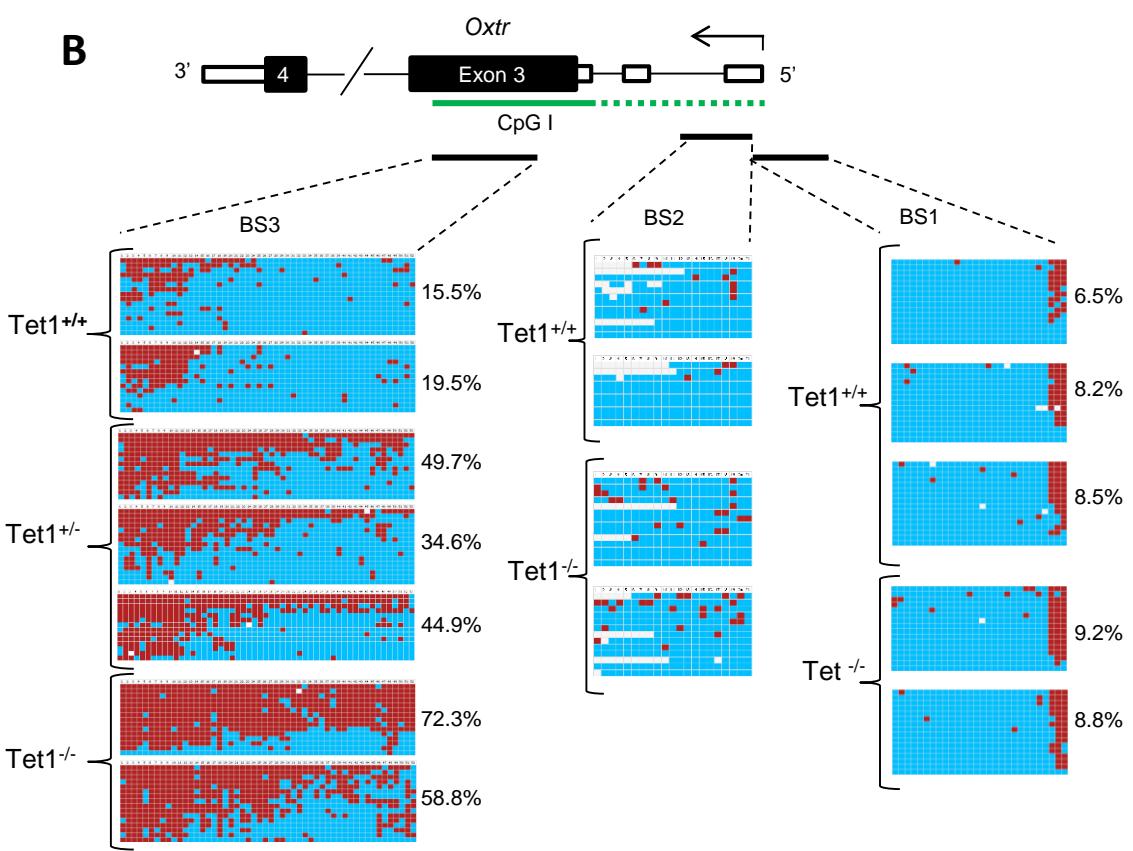
# Supplemental Figure 3



**Figure. 3: RNA-seq analysis of Tet1 mutant mice**

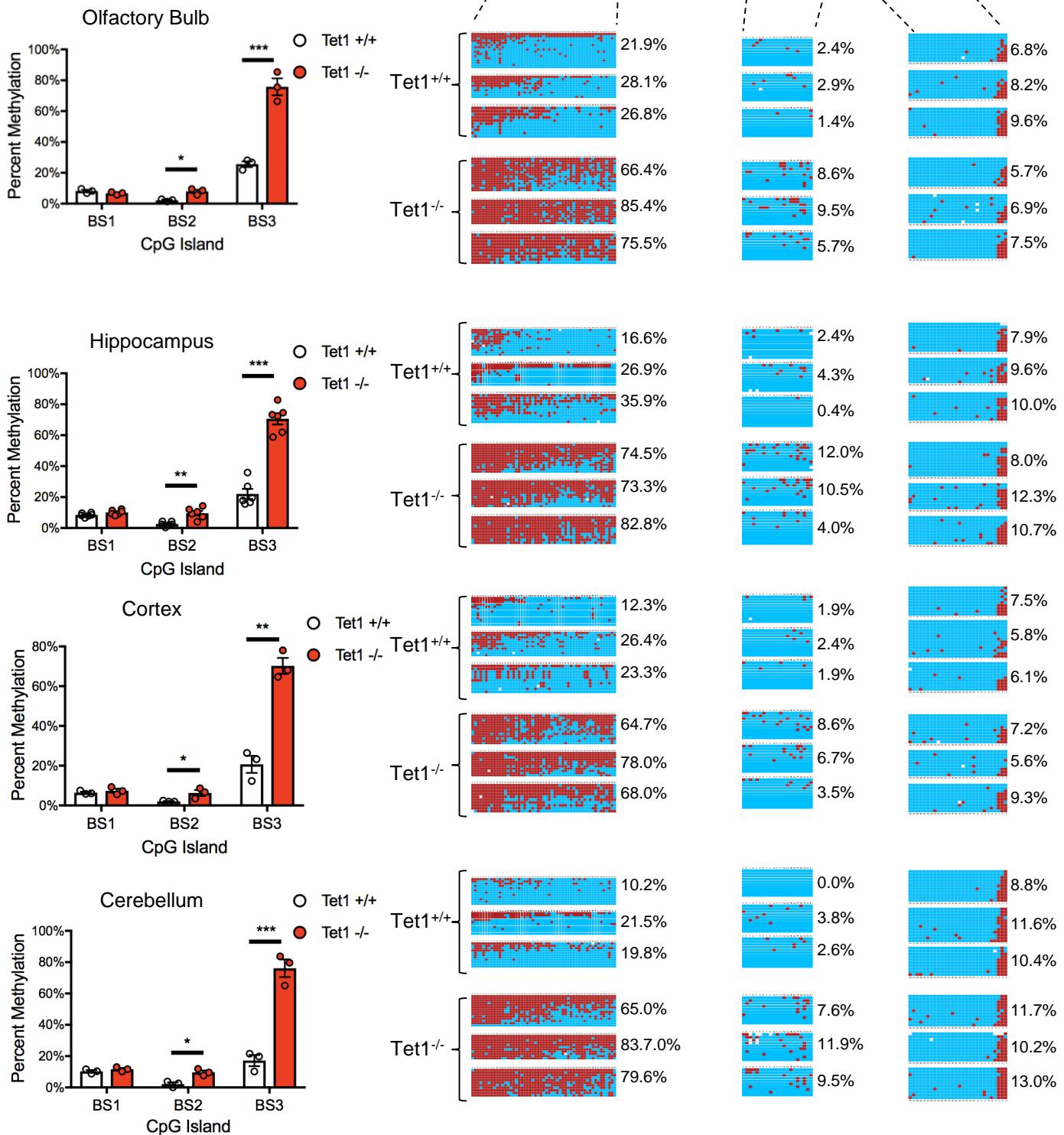
- (A) Confirmation of upregulation of activity-dependent genes (Bdnf & Homer1a) in hippocampus after electroconvulsive stimulation by qRT-PCR. n=4/group, \*\*\*, p<0.0001, two-tailed t-test.
- (B) Sequence alignment and depth of RNA-quality: Samples used in RNA-seq experiment showed high alignment and read depth
- (C) Examination of RNA sequence reads confirmed the deletion of exon 4 of Tet1 in Tet1 mutant mice

# Supplemental Figure 4

**A****B**

## **Supplemental Figure 4-continued**

C



#### **Supplemental Figure 4. Additional Bisulfite Sequencing and *Oxtr* Isoform Data**

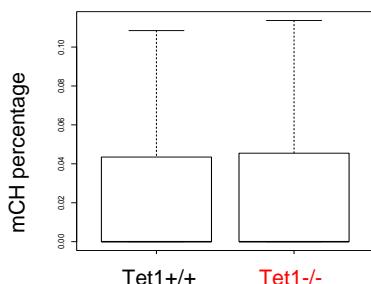
- (A) Additional hippocampal DNA methylation plots of *Npas4* CpG island from *Tet1<sup>Δe4-/-</sup>* and *Tet1<sup>+/+</sup>* mice.
- (B) Additional hippocampal DNA methylation plots of *Oxtr* BS1-3 from *Tet1<sup>Δe4-/-</sup>*, *Tet1<sup>Δe4+/-</sup>*, and *Tet1<sup>+/+</sup>* mice.
- (C) Additional DNA methylation plots show that BS2 and BS3 are hypermethylated in multiple brain regions of adult *Tet1<sup>Δe4-/-</sup>* mice. \*\*, p<0.005 ; \*\*\*, p<0.0005. All data are presented as mean ± SEM. t-test

# Supplemental Figure 5

A

Rank	Motif	Name	p	logP	q-value
1	TTGCCAAG	NF1-halfsite(CTF)/LNCaP-NF1-ChIP-Seq/Homer	1e-32	-7.474e+01	0.0000
2	GCCATCTGTT	NeuroD1(bHLH)/Islet-NeuroD1-ChIP-Seq(GSE30298)/Homer	1e-31	-7.285e+01	0.0000
3	GTACCAAGCTGGT	Atoh1(bHLH)/Cerebellum-Atoh1-ChIP-Seq/Homer	1e-29	-6.785e+01	0.0000
4	AGCAGCTG	SCL/HPC7-Scl-ChIP-Seq/Homer	1e-27	-6.421e+01	0.0000
5	ATTCCTGTC	EWS:ERG-fusion(ETS)/CADO_ES1-EWS:ERG-ChIP-Seq/Homer	1e-22	-5.150e+01	0.0000
6	CACTTCCGGT	Fli1(ETS)/CD8-FLI-ChIP-Seq(GSE20898)/Homer	1e-20	-4.736e+01	0.0000
7	AACAGCTG	MyoG(HLH)/C2C12-MyoG-ChIP-Seq(GSE36024)/Homer	1e-19	-4.505e+01	0.0000
8	ACCATCTGTT	Olig2(bHLH)/Neuron-Olig2-ChIP-Seq(GSE30882)/Homer	1e-18	-4.346e+01	0.0000
9	ACAGCTGTC	Tcf12(HLH)/GM12878-Tcf12-ChIP-Seq/Homer	1e-18	-4.298e+01	0.0000
10	CTGTTTAC	Foxo1(Forkhead)/RAW-Foxo1-ChIP-Seq/Homer	1e-17	-4.112e+01	0.0000
11	ACAGGAAGTG	ERG(ETS)/VCaP-ERG-ChIP-Seq/Homer	1e-17	-4.077e+01	0.0000
12	CACTTCCGGT	Elk4(ETS)/HeLa-Elk4-ChIP-Seq(GSE31477)/Homer	1e-16	-3.834e+01	0.0000
13	CTTGGCACGTGCCAA	NF1(CTF)/LNCAP-NF1-ChIP-Seq/Homer	1e-16	-3.824e+01	0.0000
14	AACAGGAAGT	Ets1-distal(ETS)/CD44-PoIII-ChIP-Seq/Homer	1e-16	-3.687e+01	0.0000
15	AACCGGAAAGT	ETV1(ETS)/GIST48-ETV1-ChIP-Seq/Homer	1e-15	-3.577e+01	0.0000
16	ATGACTCA	AP-1(bZIP)/ThioMac-PU.1-ChIP-Seq/Homer	1e-13	-3.003e+01	0.0000
17	CTAAAAAATAGC	Mef2c(MADS)/GM12878-Mef2c-ChIP-Seq(GSE32465)/Homer	1e-12	-2.950e+01	0.0000
18	GGCCGTCTGG	Smad4(MAD)/ESC-SMAD4-ChIP-Seq(GSE29422)/Homer	1e-12	-2.875e+01	0.0000
19	AACAGGAAAT	EWS:FLI1-fusion(ETS)/SK_N_MCES:FLI1-ChIP-Seq/Homer	1e-12	-2.858e+01	0.0000
20	CACTTCCGGT	Elk1(ETS)/HeLa-Elk1-ChIP-Seq(GSE31477)/Homer	1e-11	-2.649e+01	0.0000

B

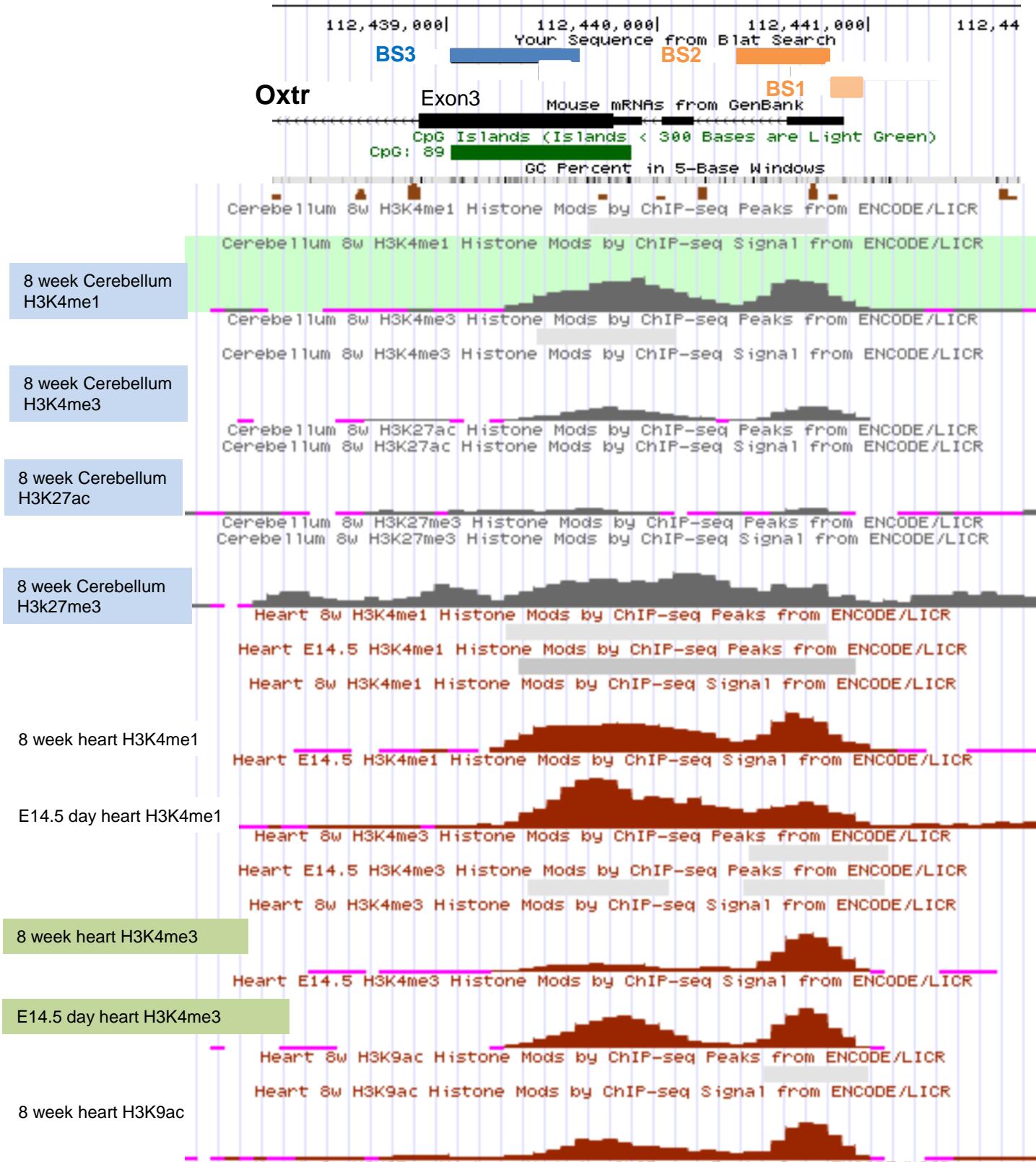


**Figure 5: DMR in Tet2-mutant mice and mCH and common motifs in DMRs of Tet1 mutant mice**

(A) Top 20 ranked motifs for in DMRs of identified in  $\text{Tet1}^{\Delta e4-/-}$  mice using HOMER2 program

(B) No significant difference for mCH methylation in between  $\text{Tet1}^{+/+}$  and  $\text{Tet1}^{\Delta e4-/-}$  mice

## Supplemental Figure 6



**Figure 6: The histone modifications at OXTR in different tissues during the development from ENCODE project.** Two peaks of various histone modifications are consistently shown in different tissue and a distinct pattern of the same histone modification, such as H3K4me3, is seen during different develop age of E14.5 and 8 week postnatally. These *in silico* data support the presence of a second potential regulator region in addition to the canonic transcription starting site for *Oxtr*. This region overlaps hypermethylated BS3 region in *Tet1<sup>Δe4/-</sup>* mice and suggest the functional role of this region via epigenetic modification.

# Supplemental Figure S7

## Behavioral cohorts and tests listed in the order performed

(Numbers of mice are indicated with Tet1 mutant genotype in parentheses).

Behavioral Test	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Conclusion
Neurophysiological screening					17(+/+) 12(-/-)	See Figure S5
Light-Dark Emergence		14(+/+) 10(-/-)				No difference except Tet1+/+ females had increased activity in 1st minute
Open Field	17(+/+) 11(-/-)	13(+/+) 10(-/-)				Tet1-/- mice are hypoactive (reduced distance traveled & rearing) and spend less time in the center
Accelerating Rotarod	17(+/+) 12(-/-)	14(+/+) 10(-/-)				Tet1-/- mice show enhanced performance
Steady-Speed Rotarod	17(+/+) 12(-/-)	14(+/+) 10(-/-)				No difference in performance between genotypes
Neurophysiological Screen	17(+/+) 12(-/-)					No difference except female Tet1-/- mice have slightly reduced grip strength
Novel Object Recognition	16(+/+) 11(-/-)	13(+/+) 10(-/-)				Tet1-/- mice trend towards impaired short-term episodic memory
Morris Water Maze	16(+/+) 11(-/-)					No difference in performance between genotypes in spatial memory and reversal
Social Transmission of Food Preference	10(+/+) 11(-/-)	8(+/+) 10(-/-)				No difference in preference between genotypes
Fear Conditioning	16(+/+) 11(-/-)	14(+/+) 10(-/-)				No difference in performance between genotypes in contextual & cued memory
Resident Intruder		14(+/+) 9(-/-)		17 (+/+) 13(-/-)		Increased threatening and stationary reactive postures in Tet1-/- females
Virgin Pup Retrieval			7(+/+) 3(-/-)	3(+/+) 4(-/-)		Delayed retrieval, decreased crouching, increased aggression in Tet1-/- females

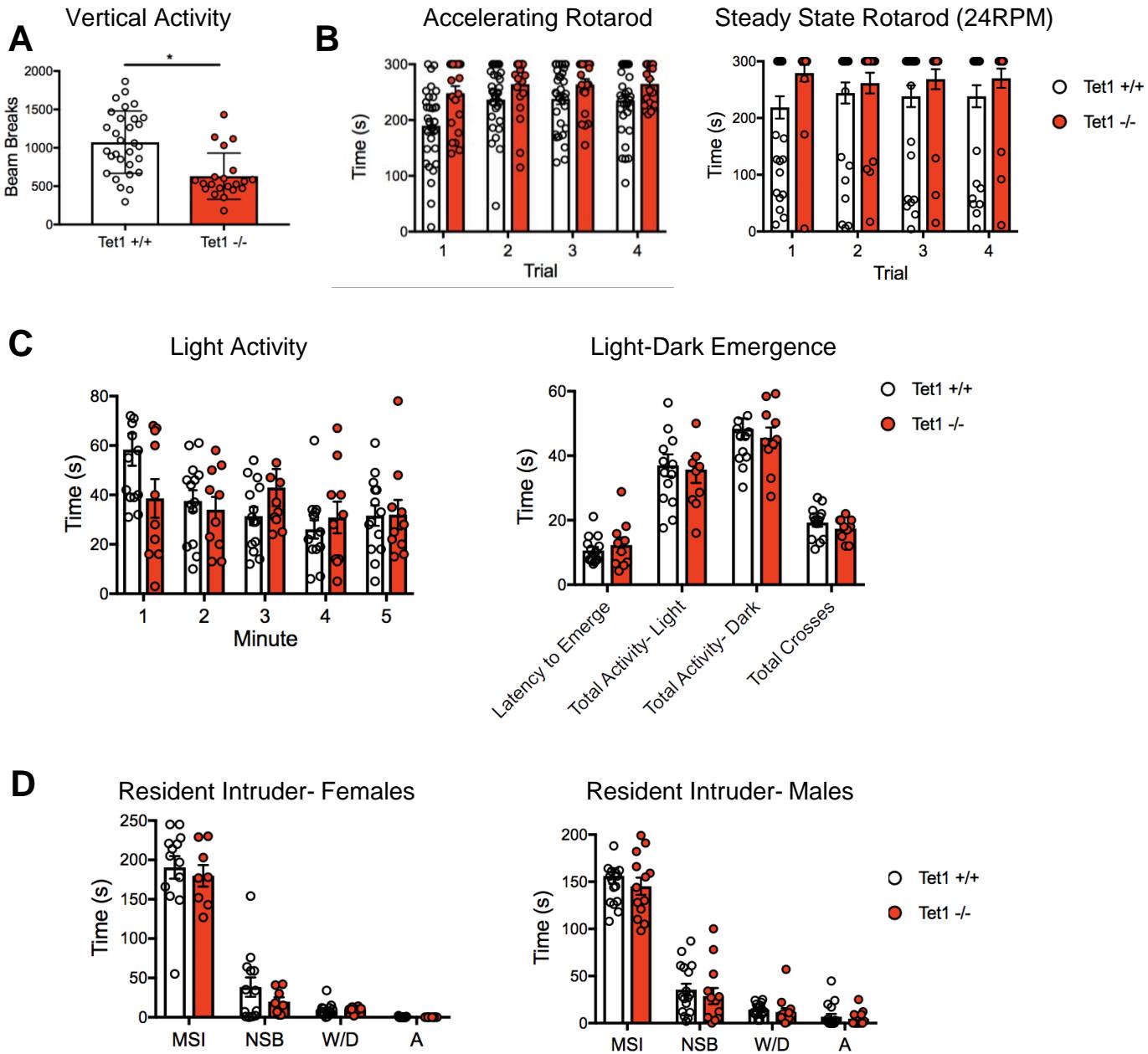
# Supplemental Figure 8

## Neurophysiological Screen of Tet1 mutant pups

	Tet1+/+ Males	Tet1-/+ Males	Tet1+/+ Females	Tet1-/+ Females
General Evaluation				
Body Posture	Normal (11/11)	Normal (7/8)	Normal (6/6)	Normal (4/4)
Tail Elevation	Normal (10/11)	Normal (7/8)	Normal (6/6)	Normal (4/4)
Pelvic Elevation	Normal (11/11)	Normal (7/8)	Normal (6/6)	Normal (4/4)
Hair Loss/Barbering	None (11/11)	None (8/8)	None (6/6)	None (4/4)
Skin Color	Normal (11/11)	Normal (8/8)	Normal (6/6)	Normal (4/4)
Body Tone	Normal (11/11)	Normal (7/8)	Normal (6/6)	Normal (4/4)
Tremor/Convulsions	Absent (11/11)	Absent (8/8)	Absent (6/6)	Absent (4/4)
Piloerection	Absent (11/11)	Absent (8/8)	Absent (6/6)	Absent (4/4)
Whiskers appearance	Normal (11/11)	Normal (8/8)	Normal (6/6)	Normal (4/4)
Ear appearance	Normal (11/11)	Normal (8/8)	Normal (6/6)	Normal (4/4)
Lacrimation	Normal (11/11)	Normal (8/8)	Normal (6/6)	Normal (3/4)
Eye appearance	Normal (11/11)	Normal (7/8)	Normal (6/6)	Normal (3/4)
No. of urination during test	0.0 ± 0.0	0.13 ± 0.13	0.17 ± 0.17	0.75 ± 0.25
No. of boli during test	0.18 ± 0.18	0.63 ± 0.26	1.5 ± 0.76	2.0 ± 0.71
Orientation/Reflexes				
Ear Reflex	Normal (11/11)	Normal (8/8)	Normal (6/6)	Normal (4/4)
Eye Reflex	Normal (9/11)	Normal (7/8)	Normal (6/6)	Normal (4/4)
Whisker Reflex	Normal (11/11)	Normal (8/8)	Normal (6/6)	Normal (4/4)
Visual Placement (cm)	2.5 ± 0.07	2.31 ± 0.09	2.42 ± 0.15	2.0 ± 0.2
Orients to moving object (%)	100 ± 0.0	100 ± 0.0	100 ± 0.0	100 ± 0.0
Hindpaw Grasp	Normal (11/11)	Normal (8/8)	Normal (6/6)	Normal (4/4)
Grip Strength				
Front Paws (g-force)	98.5 ± 4.6	98.4 ± 4.1	91.8 ± 2.2	71.9 ± 9.0*
Whole Body (g-force)	178.8 ± 5.7	179.7 ± 12.6	189.6 ± 7.0	142.3 ± 6.7**

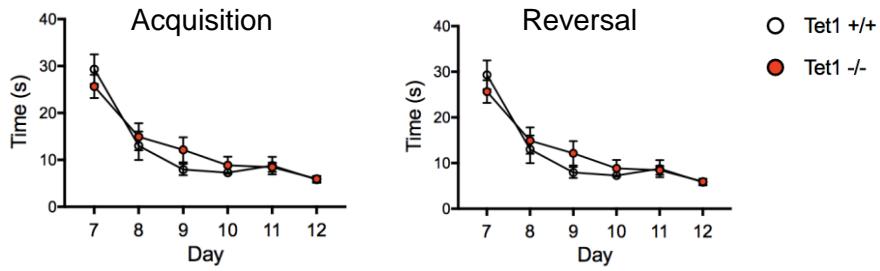
Female Tet1-/+ mice have reduced grip strength but otherwise appeared grossly normal (\*p<0.05, \*\*, p<0.005, two-tailed t-test). Numbers of mice are indicated in parentheses.

# Supplemental Figure 9

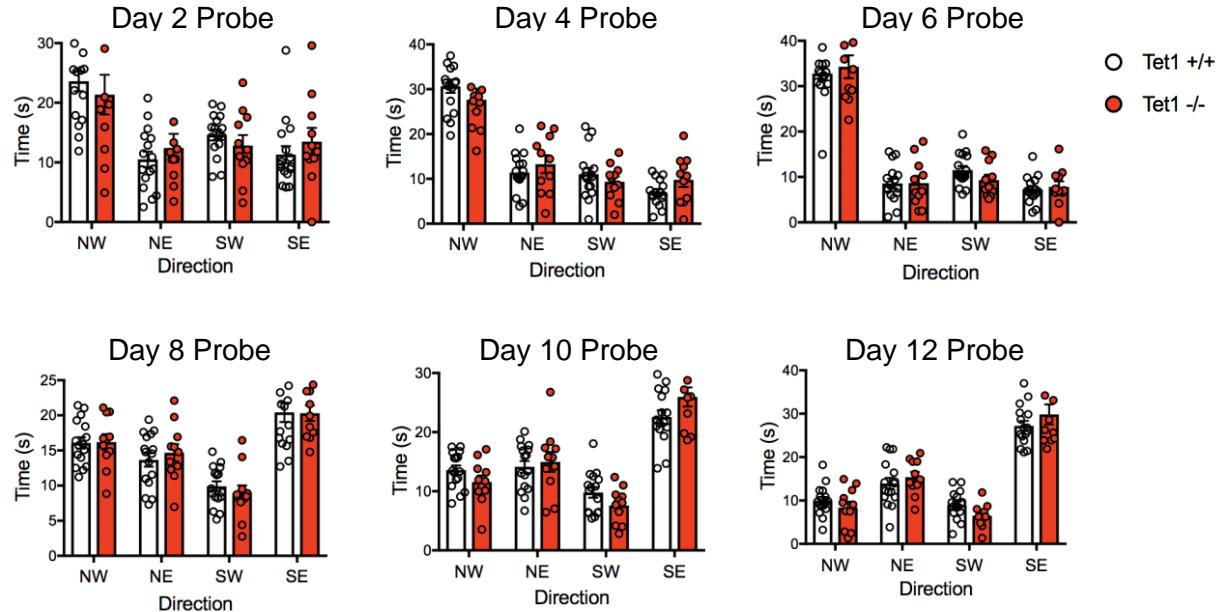


# Figure S9-continued

## E Morris Water Maze



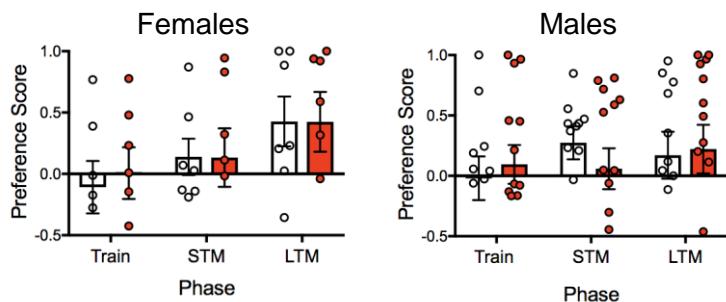
## F



## G

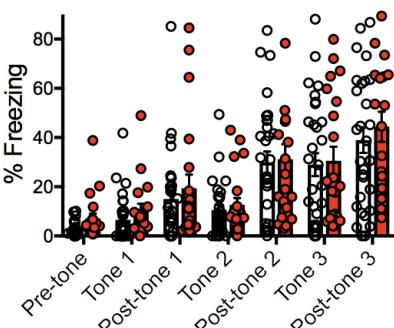
### Social Transmission of Food Preference

○ Tet1 +/+  
● Tet1 -/-

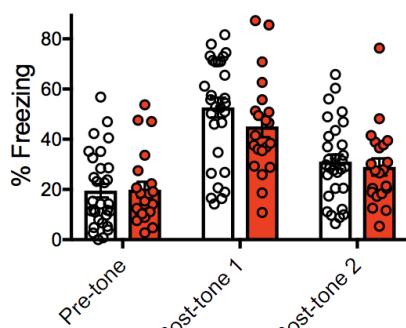


## H

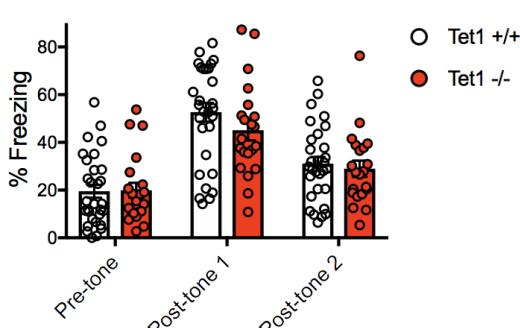
### 3x Tone & Shock



### Context Test



### Cued Test



○ Tet1 +/+  
● Tet1 -/-

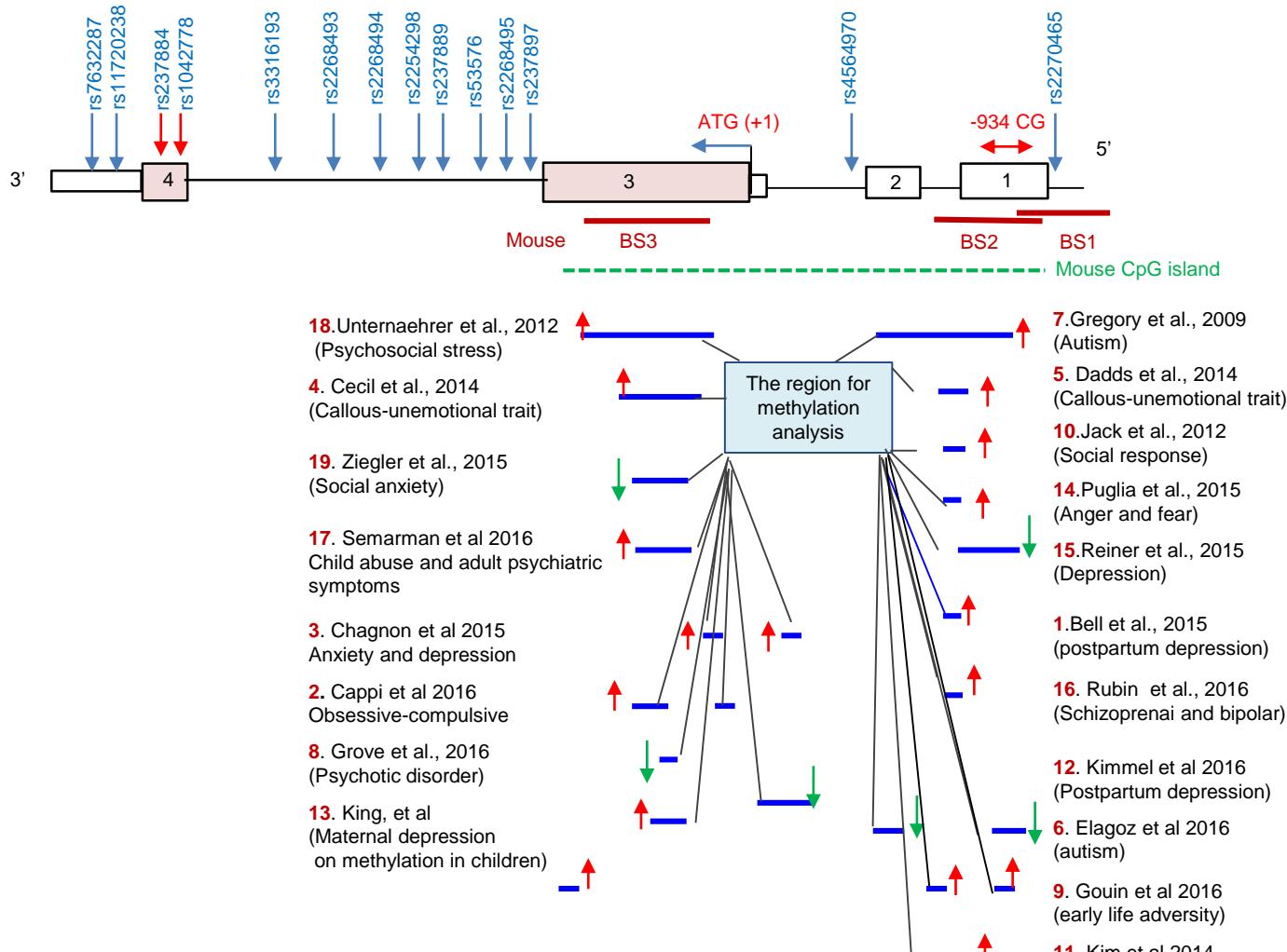
### **Figure 9. Behavioral Tests of Locomotion, Motor Learning, Anxiety, and Sociability,**

- (A) *Tet1<sup>Δe4/-</sup>* mice display significantly less vertical activity (rearing) in the open-field as measured by beam breaks. n= 21 (-/-) & 30(+/+), p=9.7E-05 , two-tailed t-test, \*p<0.05
- (B) (*left*) *Tet1<sup>Δe4/-</sup>* mice display significantly enhanced coordination on the accelerating Rotarod (4-40 RPM). [effect of time: F(3,153)=6.005, p=0.0007; effect of genotype: F(1,51)=10.11, p=0.003] (*right*) *Tet1<sup>Δe4/-</sup>* mice perform statistically similar to *Tet1<sup>+/+</sup>* in steady speed Rotarod (24RPM). n= 22 (-/-) & 31(+/+), RM-ANOVA, \*p<0.05
- (C) (*left*) *Tet1<sup>+/+</sup>* mice had increased activity in the lighted chamber during the first minute while *Tet1<sup>Δe4/-</sup>* mice had similar levels of activity throughout the 5 minute test [minute x genotype: F(4,88)=3.338, p=0.014, RM-ANOVA]. Otherwise *Tet1<sup>Δe4/-</sup>* mice performed normally in the light-dark emergence test (*right*). n= 10 (-/-) & 14 (+/+), t-test.
- (D) *Tet1<sup>Δe4/-</sup>* mice display similar levels of social investigation (MSI), non-social behaviors (NSB), withdrawal/disengagement (W/D), and attacks (A) as WT in the resident intruder test. n= 7M&8F(-/-) & 14M&13F(+/+), t-test.
- (E) *Tet1<sup>Δe4/-</sup>* mice performed similarly to WT in both acquisition and reversal of Morris water maze. n= 11 (-/-) & 16(+/+), RM-ANOVA.
- (F) *Tet1<sup>Δe4/-</sup>* (KO) mice performed similarly to WT in the probe tests of Morris water maze. NW=northwest, NE=northeast, SW=southwest, SE=southeast quadrants. n= 11 (-/-) & 16(+/+), t-test.
- (G) *Tet1<sup>Δe4/-</sup>* mice performed similarly to WT in the social transmission of food preference test. n= 14M&7F(-/-) & 11M&7F(+/+), RMANOVA.
- (H) *Tet1<sup>Δe4/-</sup>* mice display similar freezing levels as WT in the learning phase, context test, and cued test of fear conditioning. n= 21 (-/-) & 30(+/+), RMANOVA.

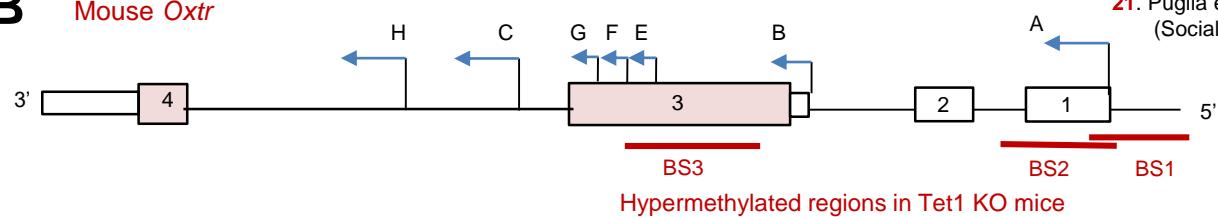
All data are presented as mean ± SEM.

# Supplemental Figure 10

## A Human OXTR



## B Mouse Oxit



**Figure 10. The association of OXTR genetic and epigenetic changes in human autism and neuropsychiatric disorders.**

- (A) Diagram of human OXTR indicating SNPs and methylated regions associated with autism spectrum disorders (ASD) and other neurobehavioral traits. Red arrows indicate increase in methylation and green arrows for reduce in methylation. The genomic region for the methylation sites and related to mouse BS2 and BS3 regions are estimated. The CG sites at +1 and -934 are cited from the reports in literate. ATG codon as +1. References for these studies are listed below
- (B) Diagram of mouse Oxit mRNA TSSs as well as the BS2 and BS3 regions which are hypermethylated in *Tet1<sup>Δe4-/-</sup>* mice.

## References for Supplemental Figure S10

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**Supplemental Table S1. Tet1Δe4/- dysregulated genes from hippocampus 2 hours after ECS**

Gene	Genomic locus	WT_FPKM	KO_FPKM	log2(fold_change)	p_value	q_value	Significant
<b>Ngp</b>	chr9:110419807-110423012	1.91142	0.0788098	-4.60013	0.0003	0.0233027	yes
<b>S100a8</b>	chr3:90669070-90670034	7.66453	0.930907	-3.04149	0.0001	0.00912687	yes
<b>Rdh7</b>	chr10:127884026-127888733	0.410831	0.0514635	-2.99692	0.00075	0.0484613	yes
<b>S100a9</b>	chr3:90692632-90695691	8.40071	1.1011	-2.93156	5.00E-05	0.00496701	yes
<b>Has1</b>	chr17:17843325-17855188	0.506307	0.0691093	-2.87306	0.0001	0.00912687	yes
<b>Gm13152</b>	chr4:147175865-147513420	1.22272	0.184397	-2.72921	5.00E-05	0.00496701	yes
<b>Wnt6</b>	chr1:74771891-74785319	0.43818	0.0666755	-2.71629	0.0001	0.00912687	yes
<b>Adh1</b>	chr3:138277644-138290691	0.92691	0.143049	-2.69592	5.00E-05	0.00496701	yes
<b>Hp</b>	chr8:109575127-109579172	0.871104	0.137302	-2.66549	5.00E-05	0.00496701	yes
<b>Ambp</b>	chr4:63143278-63154142	0.698333	0.111792	-2.64309	0.00035	0.0263456	yes
<b>Arg1</b>	chr10:24915206-24927470	0.403878	0.0672171	-2.58702	0.0007	0.0462538	yes
<b>Evp1</b>	chr11:116220558-116238091	0.337259	0.0562775	-2.58323	5.00E-05	0.00496701	yes
<b>Apoa5</b>	chr9:46268607-46271919	0.276145	0.0461177	-2.58203	0.00045	0.0325314	yes
<b>D130017N</b>	chr5:143758353-143764942	3.59233	0.636123	-2.49754	5.00E-05	0.00496701	yes
<b>Kng1</b>	chr16:23058299-23082078	0.413942	0.0783263	-2.40186	0.00015	0.0125888	yes
<b>Mup20</b>	chr4:62050234-62054117	9.34867	1.78305	-2.39042	5.00E-05	0.00496701	yes
<b>Serpina3k</b>	chr12:104338485-104345739	2.87926	0.566299	-2.34606	5.00E-05	0.00496701	yes
<b>Dsc3</b>	chr18:19960929-20002097	0.267456	0.053836	-2.31266	5.00E-05	0.00496701	yes
<b>Capn11</b>	chr17:45630203-45659309	0.416479	0.0857323	-2.28034	5.00E-05	0.00496701	yes
<b>Apoa2</b>	chr1:171225053-171226379	15.703	3.24835	-2.27326	5.00E-05	0.00496701	yes
<b>Apoa1</b>	chr9:46228629-46230466	4.93677	1.02192	-2.27228	5.00E-05	0.00496701	yes
<b>Mup7</b>	chr4:60066468-60139858	7.12571	1.55634	-2.19488	5.00E-05	0.00496701	yes
<b>Serpina1b</b>	chr12:103728155-103738189	0.830373	0.185535	-2.16207	0.0001	0.00912687	yes
<b>Henmt1</b>	chr3:108940083-108960776	0.679082	0.152106	-2.15851	5.00E-05	0.00496701	yes
<b>Serpinc1</b>	chr1:160978605-161003014	0.40564	0.09284	-2.12738	0.0001	0.00912687	yes
<b>Mup3</b>	chr4:62083475-62087312	8.77856	2.01091	-2.12613	5.00E-05	0.00496701	yes
<b>Fga</b>	chr3:83026152-83033617	0.26601	0.0614374	-2.11429	5.00E-05	0.00496701	yes
<b>Fgg</b>	chr3:83007895-83015049	0.886665	0.206003	-2.10573	5.00E-05	0.00496701	yes
<b>Slc26a10</b>	chr10:127172425-127180645	2.38848	0.566491	-2.07597	5.00E-05	0.00496701	yes
<b>Mup14</b>	chr4:61300036-61439704	2.48105	0.603117	-2.04044	5.00E-05	0.00496701	yes
<b>H2-Q10</b>	chr17:35470088-35474563	0.543287	0.133407	-2.02588	5.00E-05	0.00496701	yes
<b>Ldoc1</b>	chrX:61709615-61710950	1.78675	0.439895	-2.0221	0.0001	0.0181913	yes

<b>Cyp2e1</b>	chr7:140763831-140774977	1.76001	0.438441	-2.00513	5.00E-05	0.00496701	yes
<b>Akr1c6</b>	chr13:4434342-4457530	0.915727	0.229498	-1.99644	5.00E-05	0.00496701	yes
<b>Serpina1c</b>	chr12:103894925-103904950	0.911861	0.230218	-1.98581	5.00E-05	0.00496701	yes
<b>Fabp1</b>	chr6:71199887-71205023	6.70554	1.74072	-1.94567	5.00E-05	0.00496701	yes
<b>Apoc4</b>	chr7:19678083-19681460	1.82408	0.473755	-1.94495	0.00075	0.0484613	yes
<b>Aldh3a1</b>	chr11:61208741-61218416	0.500983	0.130663	-1.93891	0.0004	0.029501	yes
<b>Pirt</b>	chr11:66905631-66947086	1.28959	0.342654	-1.91209	5.00E-05	0.00496701	yes
<b>Zfp648</b>	chr1:154201186-154205674	0.465884	0.125917	-1.88749	0.00015	0.0125888	yes
<b>Alb</b>	chr5:90460888-90476603	9.81762	2.69402	-1.86561	5.00E-05	0.00496701	yes
<b>Lect1</b>	chr14:79637689-79662170	1.69306	0.467635	-1.85617	5.00E-05	0.00496701	yes
<b>Ahsg</b>	chr16:22892014-22899451	1.16364	0.322683	-1.85046	5.00E-05	0.00496701	yes
<b>Serpina1d</b>	chr12:103763586-103773633	0.538655	0.149413	-1.85006	0.00045	0.0325314	yes
<b>Apoc3</b>	chr9:46233050-46235297	3.31137	0.945412	-1.80841	0.00015	0.0125888	yes
<b>Apoc1</b>	chr7:19689480-19692658	10.815	3.08884	-1.8079	5.00E-05	0.00496701	yes
<b>Bhmt</b>	chr13:93616890-93637758	0.79142	0.227637	-1.79771	5.00E-05	0.00496701	yes
<b>Slc47a1</b>	chr11:61343399-61378075	0.541613	0.15696	-1.78687	0.0001	0.00912687	yes
<b>Foxc2</b>	chr8:121116170-121118894	0.306641	0.0933269	-1.71618	0.00045	0.0325314	yes
<b>Mrgprf</b>	chr7:145300908-145309557	0.404722	0.125434	-1.69001	0.00055	0.0373565	yes
<b>Hmgcs2</b>	chr3:98280430-98310738	2.61824	0.813642	-1.68613	5.00E-05	0.00496701	yes
<b>Hpx</b>	chr7:105591610-105600116	1.02879	0.325212	-1.6615	5.00E-05	0.00496701	yes
<b>Gnmt</b>	chr17:46725663-46729165	0.892059	0.284791	-1.64724	0.00055	0.0373565	yes
<b>Slc6a12</b>	chr6:121346696-121365773	0.651967	0.210858	-1.62853	5.00E-05	0.00496701	yes
<b>Fgfbp1</b>	chr5:43978857-43981799	1.00005	0.326668	-1.61418	0.0001	0.00912687	yes
<b>Cdh1</b>	chr8:106603367-106670246	0.378277	0.123825	-1.61114	5.00E-05	0.00496701	yes
<b>Mst1r</b>	chr9:107906888-107920383	0.622716	0.205234	-1.60131	5.00E-05	0.00496701	yes
<b>Alox12b</b>	chr11:69157071-69169791	2.93969	0.970358	-1.59907	5.00E-05	0.00496701	yes
<b>Gpnmb</b>	chr6:49036517-49058182	1.29643	0.435325	-1.57438	5.00E-05	0.00496701	yes
<b>Cyp3a11</b>	chr5:145854606-145879854	1.26915	0.428883	-1.5652	5.00E-05	0.00496701	yes
<b>Slc38a5</b>	chrX:8271391-8280176	2.42498	0.838801	-1.53157	5.00E-05	0.009702	yes
<b>Creb3l3</b>	chr10:81084332-81098872	0.338664	0.118559	-1.51425	0.00065	0.0433422	yes
<b>Asgr1</b>	chr11:70054368-70057894	0.739037	0.265067	-1.47929	0.00065	0.0433422	yes
<b>Gc</b>	chr5:89417510-89457898	1.07468	0.389267	-1.46508	5.00E-05	0.00496701	yes
<b>Fgb</b>	chr3:83042304-83049790	0.755294	0.273879	-1.4635	0.00015	0.0125888	yes
<b>Vill</b>	chr9:119052777-119071525	0.406663	0.148565	-1.45274	5.00E-05	0.00496701	yes

<b>Barx2</b>	chr9:31846043-31913285	0.882743	0.328986	-1.42397	0.00015	0.0125888	yes
<b>Mpzl2</b>	chr9:45042343-45054043	0.748455	0.286093	-1.38743	5.00E-05	0.00496701	yes
<b>Kctd14</b>	chr7:97451333-97459557	1.03911	0.398713	-1.38192	5.00E-05	0.00496701	yes
<b>Crabp2</b>	chr3:87948692-87953372	2.04716	0.794353	-1.36577	0.00015	0.0125888	yes
<b>C3</b>	chr17:57203972-57228136	0.404668	0.157965	-1.35713	5.00E-05	0.00496701	yes
<b>Slc22a6</b>	chr19:8617995-8628299	1.20649	0.48435	-1.31669	5.00E-05	0.00496701	yes
<b>Fmod</b>	chr1:134037514-134048277	6.92639	2.78989	-1.3119	5.00E-05	0.00496701	yes
<b>Aldh1a2</b>	chr9:71215788-71296243	3.49429	1.42599	-1.29304	5.00E-05	0.00496701	yes
<b>Gpr182</b>	chr10:127749601-127751798	1.2271	0.511308	-1.26299	5.00E-05	0.00496701	yes
<b>Clec14a</b>	chr12:58264719-58269258	0.51169	0.214081	-1.25712	5.00E-05	0.00496701	yes
<b>Col6a6</b>	chr9:105689416-105828085	0.231765	0.097923	-1.24294	5.00E-05	0.00496701	yes
<b>Anxa1</b>	chr19:20373433-20390671	1.51154	0.642882	-1.2334	0.00015	0.0125888	yes
<b>Slc6a13</b>	chr6:121300295-121337718	3.58199	1.52402	-1.23288	5.00E-05	0.00496701	yes
<b>Slc13a4</b>	chr6:35267952-35308126	3.58991	1.53989	-1.22112	5.00E-05	0.00496701	yes
<b>Tnxb</b>	chr17:34670534-34719815	1.60725	0.693652	-1.21231	5.00E-05	0.00496701	yes
<b>Ldhd</b>	chr8:111626270-111630322	6.65588	2.9232	-1.18708	5.00E-05	0.00496701	yes
<b>Ndn</b>	chr7:62348276-62349927	89.2939	40.2216	-1.15059	5.00E-05	0.00496701	yes
<b>Cyp27a1</b>	chr1:74713573-74737890	1.10332	0.499006	-1.14472	0.0001	0.00912687	yes
<b>Vmn2r29</b>	chr7:7212995-7278289	1.78836	0.831238	-1.1053	0.00015	0.0125888	yes
<b>Col3a1</b>	chr1:45311537-45349706	2.09846	0.984397	-1.09202	5.00E-05	0.00496701	yes
<b>Acta2</b>	chr19:34240335-34255373	2.53914	1.19539	-1.08686	5.00E-05	0.00496701	yes
<b>Ly6g6e</b>	chr17:35076941-35078804	1.49156	0.703862	-1.08346	0.00055	0.0373565	yes
<b>Tfr2</b>	chr5:137569850-137587481	1.93526	0.928317	-1.05984	5.00E-05	0.00496701	yes
<b>Alox8</b>	chr11:69183884-69197843	0.547904	0.264212	-1.05223	0.0005	0.034769	yes
<b>Tpm2</b>	chr4:43514711-43523388	1.5033	0.738042	-1.02636	5.00E-05	0.00496701	yes
<b>Dnahc6</b>	chr6:73017606-73221631	0.984016	0.485449	-1.01936	5.00E-05	0.00496701	yes
<b>Nek10</b>	chr14:14820814-15006693	0.697491	0.344126	-1.01924	0.00015	0.0125888	yes
<b>Cd59a</b>	chr2:104095800-104115351	1.81451	0.895518	-1.01879	0.00015	0.0125888	yes
<b>Tekt5</b>	chr16:10361253-10395448	2.68679	1.34494	-0.998337	0.00015	0.0125888	yes
<b>Hhatl</b>	chr9:121784015-121792507	3.81247	1.92101	-0.988863	5.00E-05	0.00496701	yes
<b>Rbp4</b>	chr19:38116619-38125321	7.68235	3.88327	-0.984276	5.00E-05	0.00496701	yes
<b>Col1a1</b>	chr11:94936269-94951856	4.32055	2.19365	-0.97788	5.00E-05	0.00496701	yes
<b>Vwf</b>	chr6:125552947-125686679	1.85072	0.940589	-0.976453	5.00E-05	0.00496701	yes
<b>Pgam2</b>	chr11:5801636-5803796	12.112	6.16483	-0.974305	5.00E-05	0.00496701	yes

<b>Resp18</b>	chr1:75272201-75278380	37.8293	19.2695	-0.973185	5.00E-05	0.00496701	yes
<b>Clec3b</b>	chr9:123150945-123157432	4.41398	2.25076	-0.971665	5.00E-05	0.00496701	yes
<b>Gpx3</b>	chr11:54902853-54910382	3.25772	1.67537	-0.959382	5.00E-05	0.00496701	yes
<b>Mgp</b>	chr6:136872434-136875805	28.5614	14.7564	-0.952722	5.00E-05	0.00496701	yes
<b>Pla2g4e</b>	chr2:120166411-120245335	3.2408	1.67461	-0.952523	5.00E-05	0.00496701	yes
<b>Col1a2</b>	chr6:4505696-4541543	6.22463	3.22644	-0.948045	5.00E-05	0.00496701	yes
<b>Gm13157</b>	chr4:147753973-147809788	1.1426	0.604968	-0.917386	0.00055	0.0373565	yes
<b>Spink8</b>	chr9:109816626-109826627	16.1102	8.5532	-0.91344	5.00E-05	0.00496701	yes
<b>Igf2</b>	chr7:142650767-142670356	35.2188	18.7439	-0.90993	5.00E-05	0.00496701	yes
<b>Fcrls</b>	chr3:87250964-87263524	6.43964	3.46149	-0.895585	5.00E-05	0.00496701	yes
<b>Aox3</b>	chr1:58113135-58200452	0.587033	0.31656	-0.890964	0.0005	0.034769	yes
<b>Col9a2</b>	chr4:121039565-121055325	1.82206	0.991596	-0.877745	5.00E-05	0.00496701	yes
<b>Slc22a8</b>	chr19:8591253-8611835	2.45562	1.34281	-0.870829	5.00E-05	0.00496701	yes
<b>Lyz2</b>	chr10:117277540-117282272	5.01556	2.75838	-0.862589	0.0001	0.00912687	yes
<b>Tlr9</b>	chr9:106222597-106226876	1.02106	0.562231	-0.860831	0.0002	0.0164079	yes
<b>Cd74</b>	chr18:60803848-60812652	3.17539	1.74867	-0.860679	0.00045	0.0325314	yes
<b>Itih2</b>	chr2:10094590-10130683	1.62853	0.897353	-0.859823	5.00E-05	0.00496701	yes
<b>Cd163</b>	chr6:124304650-124330527	0.886269	0.488437	-0.859571	5.00E-05	0.00496701	yes
<b>Thbs4</b>	chr13:92751585-92794818	3.72082	2.0611	-0.852206	5.00E-05	0.00496701	yes
<b>Gjb2</b>	chr14:57098601-57104702	3.24497	1.82056	-0.833819	5.00E-05	0.00496701	yes
<b>Slc13a3</b>	chr2:165405294-165473197	7.32558	4.12399	-0.828904	5.00E-05	0.00496701	yes
<b>Slc6a20a</b>	chr9:123636906-123678832	7.3581	4.2211	-0.801713	5.00E-05	0.00496701	yes
<b>Spp1</b>	chr5:104435110-104441053	5.90189	3.40882	-0.791904	5.00E-05	0.00496701	yes
<b>Pcolce</b>	chr5:137605106-137611404	3.04988	1.76255	-0.791087	0.00015	0.0125888	yes
<b>Gstm6</b>	chr3:107938847-107943749	4.17913	2.4174	-0.789749	0.0003	0.0233027	yes
<b>Mrc2</b>	chr11:105292645-105351145	1.143	0.666607	-0.777923	5.00E-05	0.00496701	yes
<b>Card10</b>	chr15:78775135-78803042	1.73204	1.0141	-0.77228	5.00E-05	0.00496701	yes
<b>Bgn</b>	chrX:73483634-73495936	7.13872	4.19509	-0.766966	5.00E-05	0.009702	yes
<b>Mid1</b>	chrX:169685246-169990797	6.40489	3.78249	-0.759838	5.00E-05	0.009702	yes
<b>Myh11</b>	chr16:14194526-14291408	0.916276	0.542931	-0.755013	0.0001	0.00912687	yes
<b>Lama1</b>	chr17:67697264-67822645	0.409616	0.243198	-0.752142	0.0004	0.029501	yes
<b>Nrsn2</b>	chr2:152345668-152376566	34.3415	20.5326	-0.742034	5.00E-05	0.00496701	yes
<b>Ptgds</b>	chr2:25466711-25469749	470.078	283.739	-0.728338	5.00E-05	0.00496701	yes
<b>1700048O1</b>	chr9:121937274-121947016	3.78028	2.29181	-0.722008	0.0003	0.0233027	yes

<b>Fam198b</b>	chr3:79885929-79946278	0.889411	0.541142	-0.716843	0.0002	0.0164079	yes
<b>Acer2</b>	chr4:86874413-86920881	2.0233	1.23173	-0.716017	5.00E-05	0.00496701	yes
<b>As3mt</b>	chr19:46707442-46741095	5.50317	3.36049	-0.711592	5.00E-05	0.00496701	yes
<b>Bmp7</b>	chr2:172869686-172940293	3.47449	2.13122	-0.705126	5.00E-05	0.00496701	yes
<b>Dnahc1</b>	chr14:31260374-31323896	0.731117	0.448763	-0.704149	5.00E-05	0.00496701	yes
<b>Col5a2</b>	chr1:45374330-45503282	2.18381	1.35619	-0.687289	5.00E-05	0.00496701	yes
<b>Tshz2</b>	chr2:169633645-169888504	8.13282	5.08563	-0.67733	5.00E-05	0.00496701	yes
<b>Col6a2</b>	chr10:76595755-76623404	3.87497	2.42598	-0.675618	5.00E-05	0.00496701	yes
<b>Fbln1</b>	chr15:85206007-85286294	3.40284	2.13615	-0.671728	5.00E-05	0.00496701	yes
<b>Erdr1</b>	chrY:90785441-90816465	36.4077	22.863	-0.671233	5.00E-05	0.009702	yes
<b>Pnma3</b>	chrX:73064786-73068191	6.98092	4.41735	-0.660236	5.00E-05	0.009702	yes
<b>Trim66</b>	chr7:109449000-109508134	1.57729	1.00015	-0.657224	5.00E-05	0.00496701	yes
<b>Ctgf</b>	chr10:24595441-24598682	4.28064	2.72393	-0.652138	0.00015	0.0125888	yes
<b>Eln</b>	chr5:134702595-134747254	6.28166	3.99822	-0.651788	5.00E-05	0.00496701	yes
<b>Zfp772</b>	chr7:7202121-7209998	2.5257	1.61187	-0.647954	0.00065	0.0433422	yes
<b>Islr</b>	chr9:58156263-58159221	5.62788	3.61516	-0.638534	5.00E-05	0.00496701	yes
<b>Lamc3</b>	chr2:31887280-31946535	1.31386	0.845161	-0.636516	0.0005	0.034769	yes
<b>Btg2</b>	chr1:134074864-134079155	13.7891	8.87802	-0.635221	5.00E-05	0.00496701	yes
<b>Rbp1</b>	chr9:98422960-98446550	2.7301	1.76532	-0.629025	0.00035	0.0263456	yes
<b>Fn1</b>	chr1:71585472-71653234	7.6798	4.97097	-0.62754	5.00E-05	0.00496701	yes
<b>Ddr2</b>	chr1:169969408-170088944	2.03071	1.31578	-0.626069	5.00E-05	0.00496701	yes
<b>Gucy1a3</b>	chr3:82092426-82145877	6.97855	4.53818	-0.620815	5.00E-05	0.00496701	yes
<b>Zic2</b>	chr14:122475383-122480328	3.43731	2.26645	-0.600845	0.00025	0.0200591	yes
<b>Gpr83</b>	chr9:14860253-14869499	5.66929	3.74428	-0.598481	5.00E-05	0.00496701	yes
<b>Ccnf</b>	chr17:24223231-24251409	4.36196	2.89144	-0.593189	5.00E-05	0.00496701	yes
<b>Ubc</b>	chr5:125385964-125390017	38.9628	25.8312	-0.592984	5.00E-05	0.00496701	yes
<b>Ptprb</b>	chr10:116301373-116389538	1.92815	1.28556	-0.584817	5.00E-05	0.00496701	yes
<b>Igfbp2</b>	chr1:72824479-72852471	18.5358	12.3656	-0.583978	5.00E-05	0.00496701	yes
<b>Pamr1</b>	chr2:102550020-102643040	3.60291	2.41327	-0.578173	0.0003	0.0233027	yes
<b>Nxph3</b>	chr11:95509845-95514565	7.56308	5.10091	-0.568218	5.00E-05	0.00496701	yes
<b>Npas4</b>	chr19:4984354-4989971	8.20781	5.58198	-0.556219	0.0002	0.0164079	yes
<b>Nid1</b>	chr13:13437601-13512275	2.24161	1.5258	-0.554967	0.00035	0.0263456	yes
<b>AI854703</b>	chr6:48628166-48633688	4.67251	3.18438	-0.553186	0.0001	0.00912687	yes
<b>Sstr1</b>	chr12:58211803-58216036	9.01341	6.18201	-0.543996	5.00E-05	0.00496701	yes

<b>Thbd</b>	chr2:148404470-148408188	6.01016	4.13976	-0.537856	0.0001	0.00912687	yes
<b>Cobl</b>	chr11:12236675-12464960	2.15945	1.48988	-0.535464	0.00055	0.0373565	yes
<b>Kcnf1</b>	chr12:17172099-17176888	20.0102	13.909	-0.524717	5.00E-05	0.00496701	yes
<b>Vtn</b>	chr11:78499119-78502325	29.8193	21.0188	-0.504567	5.00E-05	0.00496701	yes
<b>Slc5a5</b>	chr8:70882888-70892757	6.33845	4.51338	-0.48992	0.00035	0.0263456	yes
<b>Oxtr</b>	chr6:112473683-112489808	3.51661	2.51145	-0.485663	0.0005	0.034769	yes
<b>Abcb1a</b>	chr5:8660091-8748570	3.45911	2.47584	-0.48248	0.0004	0.029501	yes
<b>C4b</b>	chr17:34728380-34743897	3.48255	2.50123	-0.477504	0.00035	0.0263456	yes
<b>Grm2</b>	chr9:106644533-106656109	6.73384	4.86161	-0.469996	0.0004	0.029501	yes
<b>Lama2</b>	chr10:26981284-27616942	2.31794	1.67985	-0.464509	0.0003	0.0233027	yes
<b>Alad</b>	chr4:62505983-62520063	6.24853	4.54853	-0.458117	0.00025	0.0200591	yes
<b>Cfh</b>	chr1:140085854-140183411	5.83444	4.26587	-0.451753	0.00035	0.0263456	yes
<b>Foxo1</b>	chr3:52268336-52350109	7.66867	5.73634	-0.418847	0.0005	0.034769	yes
<b>Kcna6</b>	chr6:126708328-126740674	11.7395	8.99612	-0.383991	0.0005	0.034769	yes
<b>Oxt</b>	chr2:130576172-130576988	0.496742	0	#NAME?	5.00E-05	0.00496701	yes
<b>Retnlg</b>	chr16:48872607-48874498	0.452661	0	#NAME?	5.00E-05	0.00496701	yes
<b>Sub1</b>	chr15:11981338-11996007	77.0135	101.159	0.39344	0.0002	0.0164079	yes
<b>Pdia4</b>	chr6:47796140-47813512	20.0073	26.5276	0.406971	0.00025	0.0200591	yes
<b>Rapgef6</b>	chr11:54522844-54699286	11.9807	15.926	0.410665	0.00075	0.0484613	yes
<b>Commd6</b>	chr14:101633765-101640471	28.5892	38.307	0.42214	0.0007	0.0462538	yes
<b>Hspa5</b>	chr2:34772089-34776529	161.388	216.919	0.426623	5.00E-05	0.00496701	yes
<b>Uggt2</b>	chr14:118984984-119099434	6.57126	8.89351	0.436584	5.00E-05	0.00496701	yes
<b>Spsb1</b>	chr4:149896283-149955006	22.1226	30.1758	0.447875	0.00015	0.0125888	yes
<b>Ddo</b>	chr10:40630010-40649931	3.72712	5.16986	0.472064	0.0006	0.0405639	yes
<b>B4galt1</b>	chr4:40804581-40854537	4.50069	6.27422	0.479292	0.00025	0.0200591	yes
<b>2900052N0</b>	chr9:46913602-46927366	41.8271	59.6684	0.512529	5.00E-05	0.00496701	yes
<b>Tle1</b>	chr4:72117141-72200919	8.32706	11.8876	0.513575	5.00E-05	0.00496701	yes
<b>Gm14436</b>	chr2:175470024-175483322	3.74618	5.63788	0.589733	5.00E-05	0.00496701	yes
<b>Gm14420</b>	chr2:177464741-177479194	4.12637	6.21955	0.591938	5.00E-05	0.00496701	yes
<b>Gm14295</b>	chr2:176798599-176808704	47.5386	72.3543	0.605981	5.00E-05	0.00496701	yes
<b>Hspa1b</b>	chr17:34956428-34959238	4.67089	7.13057	0.61032	5.00E-05	0.00496701	yes
<b>Serpina3n</b>	chr12:104406707-104414329	30.0329	46.2504	0.622925	5.00E-05	0.00496701	yes
<b>Gm14403</b>	chr2:177498225-177512311	1.17629	1.82822	0.636189	0.00075	0.0484613	yes
<b>Col15a1</b>	chr4:47208011-47313165	0.593875	0.935038	0.654866	0.0005	0.034769	yes

<b>Atf3</b>	chr1:191170296-191183333	13.0752	20.6988	0.662714	5.00E-05	0.00496701	yes
<b>Gm14322</b>	chr2:177759287-177773275	3.08158	4.93664	0.679859	5.00E-05	0.00496701	yes
<b>Clcnka</b>	chr4:141384610-141398706	0.650319	1.18108	0.860886	0.0005	0.034769	yes
<b>1500015A0</b>	chr18:61726389-61728253	5.13994	9.91193	0.947415	5.00E-05	0.00496701	yes
<b>Wnk4</b>	chr11:101260566-101277409	0.977737	2.0801	1.08914	5.00E-05	0.00496701	yes
<b>C630043F0</b>	chr4:72201243-72203930	2.07202	4.77691	1.20504	5.00E-05	0.00496701	yes
<b>Prph</b>	chr15:99055173-99058978	0.503359	1.19344	1.24546	0.0001	0.00912687	yes
<b>Gm3002</b>	chr14:3814912-3830681	4.33243	11.4081	1.39681	5.00E-05	0.00496701	yes
<b>Ptchd1</b>	chrX:155569735-155623327	0.43663	1.29498	1.56845	5.00E-05	0.009702	yes
<b>Gm3558</b>	chr14:7545150-7568566	1.08873	3.67407	1.75473	5.00E-05	0.00496701	yes
<b>Gm10406</b>	chr14:7006114-7027449	0.656543	3.03727	2.20981	5.00E-05	0.00496701	yes
<b>Gm5796</b>	chr14:4023940-4041368	0.439838	2.08756	2.24678	5.00E-05	0.00496701	yes
<b>LOC10086</b>	chr14:6259746-6287250	0.295932	1.71252	2.53278	5.00E-05	0.00496701	yes
<b>Gm3893</b>	chr4:41889794-42462993	0.80983	4.81119	2.5707	5.00E-05	0.00496701	yes
<b>Gm5506</b>	chr4:150237196-150248873	3.70133	22.4101	2.59803	5.00E-05	0.00496701	yes
<b>Tuba1c</b>	chr15:99029890-99038105	0.86212	11.3096	3.71352	5.00E-05	0.00496701	yes

**Supplemental Table S2. List of neuronal activity-dependent genes from literature search**

Abcd2	Cdk5rap3	Emp1	H2-K1	Lonrf3	P4ha1	Reep1	Spsb1
Acadvl	Cdkn1a	Enah	Habp4	Lrfn1	P4ha2	Rem2	Srf
Acan	Cdkn1b	Epha2	Haghl	Lrrc3	Pak7	Rere	Srsf7
Acp1	Cds1	Eprs	Hcn1	Maff	Pam	Rerg	Sstr2
Acsl4	Chac1	Eps8	Hdac9	Magel2	Pard6a	Rgs10	St3gal1
Acss1	Chaf1a	Erf	Heca	Man1a	Pax1	Rgs2	Stac
Adamts1	Chml	Errfi1	Herpud1	Map3k2	Pcdh17	Rgs4	Stard4
Adcyap1	Chst15	Etv3	Hiat1	Map3k5	Pcdh8	Rgs7bp	Stc2
Adm	Cited1	Etv5	Hif3a	Mapk6	Pcdh9	Rhbd13	Stk40
Adora2a	Cited2	Fahd1	Hist1h1d	Mbnl2	Pcf11	Rhoq	Stxbp5
Aff1	Cldn1	Fam107b	Hist1h2bc	Mea1	Pcsk1	Ripk2	Sult2b1
Ager	Cldn25	Fam126b	Hist1h3g	Mecom	Pcsk5	Rnd3	Supt4a
Al836003	Clpb	Fam46a	Hivep3	Med14	Pde4dip	Rnf10	Suv420h2
Akr1c13	Clvs1	Fance	Homer1	Meox1	Pdk3	Rnf128	Sv2c
Alcam	Cntnap1	Fastkd5	Hpgd	Mest	Pdlim1	Rnf217	Svil
Ang	Col15a1	Fbln5	Hsd17b12	Mfap3l	Peg10	Rorb	Tac1
Ankzf1	Commd9	Fbxo18	Hsdl1	Mknk2	Peli1	Rpl22	Tacr3
Apba3	Coq10b	Fbxo33	Hspa14	Mkrn1	Per1	Rspo3	Tes
Arc	Cort	Fen1	Hspa1a	Mkrn3	Per2	Samd4	Tfcp2
Areg	Creb1	Fezf2	Hspa4	Mlf1	Pex11a	Sap30	Tgfb2
Arg2	Creld2	Fgf9	Hspa4l	Milt3	Pex13	Sars2	Tgm3
Arhgap20	Crem	Fgfr1	Hspb3	Morc4	Pfkfb4	Sc4mol	Tgoln1
Arhgap29	Crh	Fgfr2	Hspb8	Mpp3	Phf10	Sc5d	Tiparp
Arih1	Crhbp	Fkbp5	Htr5b	Mpp7	Phka2	Scg2	Tll1
Arl5b	Cryl1	Flnb	Hunk	Mpz	Pim3	Scn3a	Tmed8
Arpp21	Csrnp1	Fmn1	Ier2	Msh2	Plagl1	Scn8a	Tmem33
Arsa	Ctgf	Fndc3b	Ier3	Msh3	Plat	Sdc2	Tmem47
Asf1a	Cxxc4	Fndc9	Ifrd1	Msi2	Pld2	Serpinb2	Tmem64
Asph	Cyr61	Fos	Igddcc3	Mst1r	Plod2	Sertad1	Tmem74
Asxl1	Cyth1	Fosb	Igf1	Mthfd1l	Pnma2	Sesn2	Tmtc2
Atf3	D16Ert472e	Fosl2	Igf2bp2	Mthfd2	Pnoc	Sf1	Tmtc4
Atp10d	D3Bwg0562e	Foxk1	Il1a	Mxd4	Pold1	Sf3a2	Tnfrsf12a
Atp1b1	Dab1	Frmd6	Inhba	Mycl1	Polr2e	Sfmbt2	Tnip1
Atp2c1	Dact2	Frmpd3	Ints12	Mylk	Popdc3	Sgk1	Tob2
Atp5s	Dars	Fzd3	Invs	Myo7a	Pou3f1	Sgtb	Tpbg
Azi1	Ddit4	Fzd8	Irf1	Mypop	Ppp1r3c	Sh3rf3	Tpm3
B630005N14Rik	Ddx27	Gabpb1	Irf2bp1	Nab1	Ppp1r3e	Sik1	Traip
Baz1a	Ddx3y	Gadd45b	Itgb8	Nampt	Prkca	Sik2	Trib1
Baz2b	Dio2	Gadd45g	Itpr1	Nat6	Prkg2	Sik3	Trib3
BC022687	Dlc1	Galnt18	Itrip	Ndel1	Prok2	Sirpa	Trim66
Bdnf	Dll1	Galnt9	Jak2	Nedd9	Prox1	Sirt1	Trmt10b
Bhlhe40	Dmtf1	Gas2l3	Jmjd1c	Nek4	Prrt1	Sla	Tyk2
Boc	Dmxl1	Gch1	Jun	Nfil3	Psme4	Slc16a1	Tyro3
Bphl	Dnahc8	Gck	Junb	Nfkbid	Pten	Slc25a3	Ubfd1
Braf	Dnajb1	Gdf10	Kcna1	Nfkbiz	Ptger3	Slc25a36	Ubl3
Btg2	Dnajc1	Gem	Kcna4	Nfy	Ptger4	Slc25a37	Ubn1
Btk	Dnmt1	Gfap	Kcnf1	Nicn1	Ptgs2	Slc27a1	Unc45a
C1ql3	Dok3	Gfod1	Kcnh2	Nme6	Pthlh	Slc2a1	Usp2
C2cd4a	Dusp1	Gkap1	Kcnj3	Nnmt	Ptp4a3	Slc2a3	Usp3
C330006P03Rik	Dusp14	Gla	Kcnj4	Npas4	Ptpn20	Slc35a1	Usp9x
Cacng5	Dusp16	Gm13889	Kcnk1	Nppc	Ptpru	Slc40a1	Vgf
Cad	Dusp4	Gm5124	Kcns2	Npx2	Purb	Slc4a7	Vkorc1
Calcr1	Dusp5	Gm7120	Keap1	Nr4a1	Pvrl3	Slc5a6	Wdr54
Camk2d	Dusp6	Gmeb2	Kif18a	Nr4a2	Rab11fip2	Slc6a17	Wdr90

Cant1	E2f5	Gmpr	Kif1b	Nr4a3	Rab39	Slc6a6	Wls
Cartpt	E530001K10Rik	Gnai2	Kif22	Nrf1	Rab3c	Slc7a1	Xrcc1
Casp7	Egf	Gnb1	Kitl	Nrip3	Rabgap1l	Slc7a3	Zc3h12c
Cbln1	Egr1	Gpr12	Klf4	Nrn1	Rad51	Slc7a8	Zc3h6
Cc2d1b	Egr2	Gpr19	Klf5	Nrp1	Rai14	Slit2	Zfp105
Cckbr	Egr3	Gpr22	Klf9	Nrsn1	Ralgapa1	Snhg1	Zfp143
Ccnd3	Egr4	Gpr26	Klhl4	Nudt4	Rap1b	Snord22	Zfp688
Ccno	Ehd4	Gpr3	Lamb3	Omg	Rasa4	Sorcs3	Zfyve19
Ccnt1	Eif4ebp1	Gpr50	Leng8	Opn3	Rasgrp1	Sowahb	Zhx2
Cd34	Elac2	Gprin2	Lin7a	Osbpl3	Rbbp6	Sox12	Zkscan14
Cdc14b	Eli2	Gpt2	Lipg	Osgin2	Rbfox2	Spata2l	Zscan2
Cdc26	Elmo1	Grasp	Lmna	Otud1	Rbm11	Spry2	Zwint
Cdh11	Emd	Grk5	Lmo2	Ovca2	Rbm15	Spry4	

Column1	Column2	Column3	Column4	Column5	Column6
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Supplemental Table 3A. Tet1Δe4-22-/ DMRs in cortex by genomic locations

Promoter CpG islands		Mouse MM9 genome assembly			
chr	start	end	mCG change	gene	name
chr19	30613935	30614289	-1	Ppp1r2-ps3	
chr7	127741258	127741538	-0.78	E130201H02Rik	
chr11	58453976	58454264	-0.6	Trim58	
chr14	80061102	80061421	-0.58	Lect1	
chrX	5045048	5045348	-0.53	Mycs	
chr5	144519029	144519233	-0.53	D130017N08Rik	
chrX	138740056	138740502	-0.52	Kcne1l	
chr2	181229109	181229333	-0.5	Abhd16b	
chr8	114434000	114434233	-0.5	Chst5	
chr7	20105356	20105600	-0.47	Nkpd1	
chr13	55516181	55516491	-0.47	Pfn3	
chrX	132528316	132528624	-0.46	Arxes2	
chr11	115183145	115183361	-0.46	Ush1g	
chr16	65105370	65105616	-0.46	Htr1f	
chrX	70232622	70232903	-0.45	Zfp185	
chr7	31098952	31099178	-0.45	Alkbh6	
chr10	79344806	79344911	-0.45	Prtn3	
chr10	33847265	33847533	-0.45	Fam26f	
chr15	101242641	101243248	-0.44	Krt7	
chr5	8660244	8660528	-0.43	Abcb1a	
chr9	21992497	21992790	-0.43	Zfp872	
chr11	119873580	119873619	-0.43	Aatk	
chr1	69873437	69873776	-0.42	Spag16	
chr2	119569561	119570178	-0.42	Itpka	
chr4	106295000	106295704	-0.42	Ttc22	
chr5	144119255	144119552	-0.42	Grid2ip	
chr7	35015084	35015415	-0.42	Gpi1	
chr17	34808107	34809700	-0.41	Tnxb	
chrX	149932619	149933012	-0.4	Ubqln2	
chr1	179378404	179378451	-0.39	Zbtb18	
chr11	70428854	70429229	-0.39	Chrne	
chrX	130223169	130223620	-0.38	Pcdh19	
chr5	72971529	72972379	-0.38	Zar1	
chr7	129008507	129008725	-0.38	Scnn1b	
chr18	34879851	34880123	-0.38	Gfra3	
chr6	83036313	83036714	-0.37	Lbx2	
chr7	86762226	86762690	-0.37	Rhcg	

chr9	56712791	56713020	-0.37 Cspg4
chr11	100941030	100941364	-0.37 Hsd17b1
chr11	88107877	88108090	-0.37 1700106J16Rik
chr15	10965649	10966166	-0.37 Rxfp3
chrX	133653069	133653292	-0.36 Esx1
chr1	40382654	40382864	-0.35 Il1rl2
chr6	85075986	85076187	-0.35 Gm5878
chr11	121691489	121691895	-0.35 Ptchd3
chrX	20937941	20938198	-0.34 Gm5124
chr5	139296836	139297388	-0.34 Gm5294
chr5	110771442	110772064	-0.34 P2rx2
chr6	67325978	67326215	-0.34 Il12rb2
chr19	5503575	5503862	-0.34 1700020D05Rik
chr1	186634648	186635052	-0.33 Marc1
chr4	34136742	34137118	-0.33 Spaca1
chr15	101268972	101269452	-0.33 Krt83
chr16	16829125	16829467	-0.33 Spag6
chrX	69520042	69520495	-0.32 Gabre
chr10	87922239	87922736	-0.32 Sycp3
chrX	163819971	163820348	-0.31 Prps2
chr2	35137841	35138151	-0.31 Gsn
chr6	48579245	48579756	-0.31 Al854703
chr7	29957798	29957908	-0.31 Ggn
chr9	21794336	21794662	-0.31 Ccdc151
chrX	156828610	156828909	-0.3 Gpr64
chr2	118082505	118082743	-0.3 Fsip1
chr5	72978213	72978847	-0.3 Gm5868
chr11	120469828	120470234	-0.3 Npb
chr11	31865601	31866053	-0.29 4930524B15Rik
chrX	101608980	101609271	-0.28 Abcb7
chrX	53708566	53709152	-0.28 Ddx26b
chr3	108742960	108743361	-0.28 Henmt1
chr5	33446859	33447262	-0.28 Slc5a1
chr6	112439018	112439877	-0.28 Oxtr
chr7	142602161	142602484	-0.28 Foxi2
chr7	51568056	51568133	-0.28 Shank1
chr8	72897306	72897555	-0.28 Comp
chr9	123124807	123125195	-0.28 Cdcp1
chr9	108242148	108242420	-0.28 Gpx1
chr17	35530983	35532038	-0.28 H2-Q5
chr19	3414320	3414596	-0.28 Gal

chrX	91969837	91971870	-0.27 Zxdb
chr1	75381493	75381755	-0.27 Speg
chr7	139346110	139346399	-0.27 Cpxm2
chr8	74213045	74213400	-0.27 Insl3
chr17	23879083	23879721	-0.27 Kremen2
chr5	108877649	108877925	-0.26 Mfsd7a
chr9	54134191	54134725	-0.26 Gldn
chr11	117722024	117722229	-0.26 Tmem235
chr11	98247994	98248196	-0.26 Pnmt
chr11	73142996	73143253	-0.26 Spata22
chr12	112509272	112510208	-0.26 Amn
chr18	36924869	36925196	-0.26 Dnd1
chrX	131543354	131543645	-0.25 Zmat1
chrX	103414785	103415223	-0.25 Taf9b
chr1	33963833	33964087	-0.25 Bend6
chr5	138086336	138086713	-0.25 Irs3
chr5	115569016	115569271	-0.25 Acads
chr7	151361369	151361804	-0.25 Shank2
chr7	104548475	104548897	-0.25 Ndufc2
chr11	115184676	115185013	-0.25 Otop2
chr12	81859202	81860412	-0.25 Ccdc177
chrX	165757912	165758642	-0.24 Hccs
chrX	162917414	162917671	-0.24 Rab9
chr3	36962422	36962785	-0.24 Adad1
chr7	69493139	69493630	-0.24 Ndn
chr8	122157080	122157297	-0.24 Kcng4
chr8	109674413	109674911	-0.24 Cyb5b
chr17	68623099	68623317	-0.24 L3mbtl4
chrX	147778700	147779409	-0.23 Fam120c
chr2	164774694	164775337	-0.23 Mmp9
chr9	121686887	121687648	-0.23 Klhl40
chr9	62129872	62130100	-0.23 Spesp1
chr11	61191378	61191657	-0.23 Slc47a1
chr12	3891226	3891634	-0.23 Dnmt3a
chr19	18824186	18824502	-0.23 Trpm6
chrX	106208672	106208980	-0.22 Hmggn5
chrX	91881410	91881902	-0.22 Gspt2
chrX	72376056	72376564	-0.22 Mpp1
chr4	120712214	120712421	-0.22 Col9a2
chr7	52894078	52894323	-0.22 Rasip1
chr7	24867082	24867331	-0.22 Zfp180

chr7	4103046	4103347	-0.22	Cdc42ep5
chr8	87225456	87225799	-0.22	Lyl1
chr8	72409905	72410192	-0.22	Cilp2
chr11	72127890	72128134	-0.22	Fbxo39
chr14	14845769	14846042	-0.22	Atxn7
chr17	43766668	43767374	-0.22	Tdrd6
chrX	139400327	139401551	-0.21	Ammecr1
chrX	132420337	132420797	-0.21	Bhlhb9
chrX	101866044	101866316	-0.21	Zdhhc15
chrX	72823105	72823448	-0.21	Rab39b
chr2	157385786	157386317	-0.21	Nnat
chr4	151500534	151500754	-0.21	Espn
chr6	58856717	58857141	-0.21	Nap1l5
chr8	119516959	119517525	-0.21	Gcsh
chr12	88443063	88443537	-0.21	Ngb
chr18	61195329	61196133	-0.21	Cdx1
chr18	52688256	52689247	-0.21	Lox
chrX	162676759	162677401	-0.2	Gpm6b
chrX	160198816	160199044	-0.2	1700045I19Rik
chrX	94267831	94268035	-0.2	Pgr15l
chrX	20265392	20265947	-0.2	Cdk16
chr2	31742692	31743152	-0.2	Lamc3
chr4	125825741	125826924	-0.2	Eva1b
chr7	29163390	29163636	-0.2	Zfp36
chr8	86566208	86566552	-0.2	Il27ra
chr9	62525498	62525747	-0.2	Itga11
chr10	115855156	115855453	-0.2	1700058G18Rik
chr14	55733272	55734264	-0.2	Jph4

### Intragenic CpG islands

chr	start	end	mCG change	gene name
chr18	53711994	53712223	-0.87	Prdm6
chr11	116094058	116094296	-0.85	Evpl
chr16	48750311	48750534	-0.83	Trat1
chr6	114688315	114688639	-0.8	Atg7
chr5	150099039	150099373	-0.76	Alox5ap
chr5	121081239	121081450	-0.76	Ccdc42b
chr10	122239331	122239668	-0.67	Ppm1h
chr2	24534503	24535045	-0.66	Cacna1b
chr12	81269316	81269618	-0.66	Actn1
chr8	125154610	125154862	-0.65	Cbfa2t3

chr6	125311741	125312008	-0.63 Tnfrsf1a
chr8	3476035	3476340	-0.63 1700019B03Rik
chr11	97413068	97413297	-0.63 Srcin1
chr1	106890485	106891033	-0.59 Cdh20
chr11	83256196	83256420	-0.57 Mmp28
chrX	131570539	131570752	-0.55 3632454L22Rik
chr2	164239860	164240112	-0.55 Rbpjl
chr5	52759561	52760180	-0.55 Sod3
chr7	149268099	149268647	-0.55 Dusp8
chr7	13846330	13846931	-0.54 6330408A02Rik
chr2	151796271	151796613	-0.53 Fam110a
chr3	88991084	88991401	-0.5 Fam189b
chr7	151864382	151864853	-0.5 Ano1
chr7	127647929	127648144	-0.5 Abca16
chr18	65243300	65243684	-0.5 Nedd4l
chr16	92605845	92606378	-0.49 Runx1
chr7	148480525	148480753	-0.48 Drd4
chrX	68304162	68304464	-0.47 Mamld1
chr1	156051967	156052668	-0.47 Zfp648
chr2	163201346	163202121	-0.47 Jph2
chr11	97324701	97324920	-0.47 Arhgap23
chr17	87533254	87533497	-0.47 Soc5
chr1	136884093	136884650	-0.46 Lgr6
chr5	92821366	92821664	-0.46 Art3
chr8	87140975	87141228	-0.46 Cacna1a
chr13	55521962	55522193	-0.46 F12
chr19	47388515	47388857	-0.46 Sh3pxd2a
chr5	118687231	118687447	-0.45 Rnft2
chr17	28212974	28213327	-0.45 Tcp11
chr10	12660984	12661600	-0.44 Stx11
chr11	58948024	58949860	-0.44 Obscn
chr11	48663043	48663249	-0.44 Trim7
chr4	126891901	126892225	-0.43 Dlgap3
chr8	111480472	111480924	-0.43 Zfhx3
chr10	7587137	7587548	-0.43 Zc3h12d
chr14	22505847	22506141	-0.43 Dupd1
chr16	38484265	38484485	-0.43 Cd80
chrX	20425758	20425969	-0.42 Araf
chr4	128900643	128900906	-0.42 C77080
chr4	117540557	117540850	-0.42 Slc6a9
chr7	16744100	16744429	-0.42 Slc8a2

chr15	74359661	74359968	-0.42 Bai1
chr5	120316917	120317136	-0.41 Tbx5
chr5	23830773	23831084	-0.41 Kcnh2
chr6	114820856	114821089	-0.41 Vgll4
chr7	109255424	109255760	-0.41 Art1
chr10	60148695	60149089	-0.41 Cdh23
chr13	43295830	43296123	-0.41 Gfod1
chr5	114037668	114038059	-0.4 Wscd2
chr7	146212626	146212831	-0.4 Jakmip3
chr9	56468460	56469001	-0.4 Lingo1
chr11	63702639	63703180	-0.4 Hs3st3b1
chr11	48982620	48983138	-0.4 Btnl9
chr11	3605403	3605647	-0.4 Osbp2
chr13	43296340	43296587	-0.4 Gfod1
chr14	35636065	35636266	-0.4 Grid1
chrX	98580045	98580342	-0.39 Gjb1
chr3	96488762	96489026	-0.39 Ankrd35
chr7	4658861	4659076	-0.39 Tmem150b
chr11	33580415	33580640	-0.39 Kcnip1
chr17	71011913	71012125	-0.39 Dlgap1
chr7	19955213	19955645	-0.38 Ppp1r13l
chr9	59450839	59451170	-0.38 Celf6
chr12	113012604	113012834	-0.38 Klc1
chr4	131669417	131669895	-0.37 Oprd1
chr17	45671755	45672078	-0.37 Tcte1
chr1	38266910	38267190	-0.36 Aff3
chr2	37641959	37642411	-0.36 Crb2
chr2	6021404	6022069	-0.36 Proser2
chr4	124667303	124667505	-0.36 Rspo1
chr6	54893908	54894329	-0.36 Nod1
chr7	39006524	39006827	-0.36 Plekhf1
chr8	72610727	72611029	-0.36 Hapl4n4
chr11	103656789	103657103	-0.36 Wnt3
chr12	77253494	77253749	-0.36 Esr2
chr17	32629255	32629548	-0.36 Cyp4f39
chr17	23943885	23944141	-0.36 Srrm2
chr11	101126462	101126756	-0.35 Wnk4
chr15	79832067	79832286	-0.35 Pdgfb
chr17	85075378	85075666	-0.35 Abcg5
chr19	5756849	5757201	-0.35 Ltbp3
chr1	95298023	95298229	-0.34 Ano7

chr7	108445279	108445481	-0.34 Atg16l2
chr7	53074757	53075428	-0.34 Kcnj14
chr7	29581654	29581956	-0.34 Rinl
chr8	87240008	87240266	-0.34 Nfix
chr8	72900109	72900665	-0.34 Comp
chr10	58685969	58686179	-0.34 Sowahc
chr11	96999958	97000348	-0.34 Tbkbp1
chr11	60960735	60961151	-0.34 Tnfrsf13b
chr16	35660095	35660750	-0.34 Sema5b
chr16	13868112	13868470	-0.34 Pdxdc1
chr17	56567392	56567596	-0.34 Ptprs
chr19	10500842	10501133	-0.34 Syt7
chr19	5081794	5082054	-0.34 Tmem151a
chr15	8586128	8586335	-0.33 Slc1a3
chr16	50045927	50046133	-0.33 Gm4827
chr4	147645551	147646239	-0.32 Ptchd2
chr10	79594169	79594979	-0.32 Dos
chr11	97200213	97200448	-0.32 Gpr179
chr19	25696874	25697198	-0.32 Dmrt3
chr2	163164901	163165759	-0.31 Jph2
chr8	73899634	73900171	-0.31 Nr2f6
chr9	37237147	37237367	-0.31 Robo3
chr10	80795201	80795932	-0.31 Tbx2r
chr11	104432750	104432971	-0.31 Myl4
chr11	76250457	76250715	-0.31 Abr
chr15	76555151	76555525	-0.31 Arhgap39
chr19	6929886	6930159	-0.31 Ccdc88b
chrX	7752794	7753293	-0.3 Tbc1d25
chr1	193809114	193809379	-0.3 Rd3
chr1	58770228	58770501	-0.3 Cflar
chr6	124811171	124811384	-0.3 Gpr162
chr18	84184858	84185068	-0.3 Tshz1
chr19	21867192	21867433	-0.3 Tmem2
chr7	147256218	147256610	-0.29 Caly
chr7	135153433	135153916	-0.29 Trim72
chr9	106553128	106553343	-0.29 Grm2
chr11	116830353	116830595	-0.29 Mgat5b
chr11	103672646	103672936	-0.29 Wnt3
chr13	113622188	113622407	-0.29 Ppap2a
chr15	78502369	78503078	-0.29 Elfn2
chr1	173984132	173984379	-0.28 Nhlh1

chr1	36326076	36326542	-0.28 Neurl3
chr3	91828440	91828925	-0.28 Pglyrp3
chr5	140449093	140449449	-0.28 Elfn1
chr5	129287597	129287984	-0.28 Rimbp2
chr7	148879445	148879724	-0.28 Muc2
chr11	103195113	103195627	-0.28 Arhgap27
chr11	100126857	100127060	-0.28 Krt42
chr12	58676925	58677593	-0.28 4921506M07Rik
chr5	138716713	138717274	-0.27 Gpc2
chr7	28442922	28443469	-0.27 Map3k10
chr12	110271441	110272573	-0.27 Begain
chr13	96106085	96106500	-0.27 Zbed3
chr15	89388203	89388852	-0.27 Shank3
chr17	26568748	26569262	-0.27 Neurl1b
chrX	11729669	11729955	-0.26 2900008C10Rik
chr4	134062847	134063057	-0.26 Paqr7
chr4	107693786	107694004	-0.26 Podn
chr5	73524501	73524737	-0.26 Fryl
chr9	21752008	21752267	-0.26 BC018242
chr10	10408975	10409196	-0.26 Grm1
chr11	82247745	82248585	-0.26 Tmem132e
chr11	77281287	77281544	-0.26 Coro6
chr11	66908044	66908274	-0.26 Myh3
chr13	53214061	53214295	-0.26 Ror2
chr16	43618510	43618747	-0.26 Zbtb20
chr1	93241034	93242394	-0.25 Espnl
chr6	83092278	83092529	-0.25 Rtkn
chr7	52118872	52119167	-0.25 Ptov1
chr9	123065936	123066227	-0.25 Clec3b
chr9	21490366	21490587	-0.25 Smarca4
chr10	79075026	79075237	-0.25 C2cd4c
chr11	33022877	33023337	-0.25 Fgf18
chr16	21926343	21926557	-0.25 Map3k13
chr18	32098653	32099030	-0.25 Lims2
chrX	130221160	130222396	-0.24 Pcdh19
chr1	108609070	108609524	-0.24 Bcl2
chr4	141033367	141033685	-0.24 Spen
chr5	138015871	138016074	-0.24 Tfr2
chr5	134697600	134698100	-0.24 Ncf1
chr5	132092267	132092618	-0.24 Auts2
chr5	110530360	110530938	-0.24 Plcxd1

chr7	109261791	109262131	-0.24 Chrna10
chr7	6141145	6141513	-0.24 Zfp444
chr11	116083249	116084372	-0.24 Evpl
chr11	101125092	101125308	-0.24 Wnk4
chr11	100437670	100437932	-0.24 Cnp
chr11	49447493	49447903	-0.24 Flt4
chr18	76305359	76305914	-0.24 Zbtb7c
chr19	41450440	41450676	-0.24 Pik3ap1
chr1	136195472	136196027	-0.23 Ppfia4
chr5	143194446	143194786	-0.23 Slc29a4
chr6	113708998	113709219	-0.23 Atp2b2
chr9	58094835	58095063	-0.23 Pml
chr10	25178359	25179027	-0.23 Epb4.1l2
chr12	112661665	112662206	-0.23 Exoc3l4
chr15	76497367	76497740	-0.23 Kifc2
chr16	96380700	96381341	-0.23 Lca5l
chr17	56568238	56568620	-0.23 Ptprs
chr17	26575621	26576296	-0.23 Neurl1b
chr3	78870494	78870701	-0.22 Rapgef2
chr4	154357945	154358147	-0.22 Plch2
chr4	151654021	151654277	-0.22 Gpr153
chr6	84084923	84085131	-0.22 Dysf
chr7	71413276	71413501	-0.22 Trpm1
chr7	19979387	19979661	-0.22 Ercc2
chr8	127420197	127420402	-0.22 Exoc8
chr9	63801388	63801848	-0.22 Smad6
chr14	66349570	66349904	-0.22 Scara5
chr15	100598910	100599234	-0.22 Slc4a8
chr15	76462249	76462570	-0.22 Tonsl
chr16	17804328	17804696	-0.22 Scarf2
chr17	32552772	32553053	-0.22 Pglyrp2
chr3	81877707	81878056	-0.21 Gucy1b3
chr4	141020327	141020534	-0.21 Zbtb17
chr4	48565394	48565717	-0.21 Msantd3
chr5	135517838	135518064	-0.21 Stx1a
chr5	115932806	115933115	-0.21 Sirt4
chr6	47854638	47855349	-0.21 Zfp282
chr7	25217216	25218314	-0.21 Irgc1
chr7	19651053	19651370	-0.21 Rspn6a
chr8	112472009	112472486	-0.21 Marveld3
chr8	73366482	73366730	-0.21 Kcnn1

chr9	107095857	107096237	-0.21 Dock3
chr9	45480696	45480999	-0.21 Dscaml1
chr10	80350986	80351319	-0.21 Tmprss9
chr11	95439290	95439719	-0.21 Ngfr
chr15	25643540	25643944	-0.21 Myo10
chr17	29979028	29979320	-0.21 Mdga1
chr19	5082454	5082810	-0.21 Tmem151a
chr4	151406451	151406770	-0.2 Tas1r1
chr5	102366357	102366574	-0.2 Wdfy3
chr7	95278697	95279205	-0.2 Grm5
chr7	30577855	30578370	-0.2 Zfp30
chr7	25162318	25162657	-0.2 Kcnn4
chr7	20011431	20011683	-0.2 Mark4
chr9	121578506	121578756	-0.2 Vipr1
chr9	106549816	106550162	-0.2 Grm2
chr10	18251272	18251567	-0.2 Nhsl1
chr14	34164280	34164706	-0.2 Arhgap22
chr15	88898011	88899044	-0.2 Panx2

**Supplemental Table S3B Tet1 Δe4-/ DMRs in cortex by level of methylation**  
**Hypermethylated DMRs in Tet1Δe4-/ mice (mm9 mouse genome assembly)**

Chr	Start	End	False discovery rate (-log10(p-value))
Column1	Column2	Column3	Column4
chr10	7587100	7589100	3.193025054
chr10	10408900	10410900	1.73508702
chr10	12661100	12663100	4.752984653
chr10	41404300	41406300	2.158356588
chr10	43497500	43499500	2.713295595
chr10	60148500	60150500	2.15381786
chr10	61970500	61972500	2.410229794
chr10	79075100	79077100	1.843560506
chr10	79476700	79478700	2.197304994
chr10	79594500	79596500	3.255293512
chr10	80270900	80272900	1.926937587
chr10	80656700	80658700	2.683284225
chr10	80795100	80797100	3.224110232
chr10	80826700	80828700	1.989382959
chr10	83887900	83889900	2.513489824
chr10	115908100	115910100	2.529605949
chr10	116482500	116484500	5.085126846
chr10	120741500	120743500	2.524141991
chr10	120818500	120820500	2.375548601
chr10	120831300	120833300	1.639733495
chr10	121885300	121887300	2.944870183
chr10	126527700	126529700	2.37987746
chr10	126615300	126617300	2.081303998
chr10	127186500	127188500	1.50506044
chr11	7111500	7113500	1.931528306
chr11	11925900	11927900	2.7269006
chr11	48982700	48984700	5.35826597
chr11	49447500	49449500	2.449584564
chr11	51711900	51713900	2.321820326
chr11	57650300	57652300	1.604024506
chr11	58454100	58456100	4.205186106
chr11	58948100	58950100	5.156917936
chr11	59125700	59127700	1.827277198
chr11	60960900	60962900	3.547693289
chr11	61191100	61193100	2.454752269
chr11	69010900	69012900	1.716387
chr11	69693300	69695300	1.702268178
chr11	70428900	70430900	2.652480361
chr11	71856300	71858300	3.097396372
chr11	74978900	74980900	3.492232683

chr11	88664700	88666700	2.736351263
chr11	94326100	94328100	2.248889427
chr11	94426300	94428300	2.519858001
chr11	94984500	94986500	1.836767849
chr11	95011300	95013300	2.325910727
chr11	95695700	95697700	2.032445479
chr11	96959700	96961700	1.52432613
chr11	98247900	98249900	2.156919437
chr11	99278500	99280500	3.599875197
chr11	99854900	99856900	3.463986045
chr11	101123900	101125900	1.967559087
chr11	101967900	101969900	2.451149703
chr11	102007500	102009500	2.681829461
chr11	102170700	102172700	2.160233247
chr11	108802100	108804100	2.298614165
chr11	109226900	109228900	1.594798469
chr11	115179300	115181300	2.528508708
chr11	115183100	115185100	2.722851869
chr11	116010300	116012300	1.632298977
chr11	116142700	116144700	1.945436299
chr11	116953300	116955300	3.267662141
chr11	118716300	118718300	1.757735107
chr11	119873300	119875300	1.958392
chr11	120469900	120471900	2.806837547
chr11	120573900	120575900	1.596555691
chr12	11157900	11159900	2.310484464
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chr12	20238500	20240500	1.826021726
chr12	77506300	77508300	2.28023074
chr12	81858900	81860900	3.224800508
chr12	86481300	86483300	2.347755369
chr12	109165700	109167700	1.421577259
chr12	109543500	109545500	1.944614459
chr12	110697100	110699100	2.635477321
chr12	112509300	112511300	2.354001701
chr12	112686100	112688100	1.756464003
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chr12	113393300	113395300	1.697961074
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chr13	47241100	47243100	2.121854113
chr13	55934500	55936500	1.815735012

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chr13	58624500	58626500	2.737292719
chr13	99464700	99466700	1.835717587
chr13	111189300	111191300	2.726492323
chr13	114403500	114405500	3.500989066
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chr14	33276100	33278100	1.931374791
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chr14	67990900	67992900	2.575405568
chr14	68226300	68228300	3.540725594
chr14	79700300	79702300	2.463154348
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chr14	119321700	119323700	1.846463175
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chr15	66793300	66795300	1.600515185
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chr15	89207100	89209100	3.635166234
chr15	89359900	89361900	2.196708012
chr15	89377700	89379700	1.83689102
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chr2	164773900	164775900	2.169983273
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chr2	169004100	169006100	1.491160879
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chr2	174152500	174154500	4.334814582
chr2	180234300	180236300	1.851051478
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chr4	125826500	125828500	3.934671941
chr4	126415500	126417500	1.477068606
chr4	126891700	126893700	3.385816172
chr4	126900300	126902300	2.157315314

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chr4	128900700	128902700	1.903253318
chr4	129849500	129851500	1.981867769
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chr4	139199300	139201300	1.76364448
chr4	140374300	140376300	2.600583537
chr4	140803100	140805100	1.659921093
chr4	140865900	140867900	1.446201149
chr4	141156100	141158100	3.076232365
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chr4	147644500	147646500	3.666071013
chr4	148324500	148326500	3.532297639
chr4	148933900	148935900	1.520755908
chr4	149023900	149025900	2.538357147
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chr4	151532500	151534500	1.947937389
chr4	151558100	151560100	1.633403243
chr4	154176500	154178500	2.995000853
chr4	154268500	154270500	1.57396864
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chr5	26333500	26335500	2.400122631
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chr5	53649500	53651500	2.473706711
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chr5	74522300	74524300	2.448882517
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chr5	105908900	105910900	1.679598809
chr5	106160300	106162300	2.336819286
chr5	110909700	110911700	6.241829609
chr5	113776100	113778100	3.990410714
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chr5	119326900	119328900	1.807921606
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chr5	123401500	123403500	3.140676279
chr5	124562300	124564300	3.074818283
chr5	124643700	124645700	1.488729476
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chr5	139296100	139298100	3.362527468
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chr7	29125700	29127700	1.503685656
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chr8	38056500	38058500	2.027572163
chr8	47586500	47588500	2.032839615
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chr8	66430700	66432700	2.447481461
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chr8	72899500	72901500	3.577236354
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chr8	108144100	108146100	2.049444692
chr8	111480500	111482500	2.226554548

chr8	113889900	113891900	2.593467418
chr8	122515900	122517900	2.383668805
chr8	123331100	123333100	1.570287519
chr8	123495900	123497900	2.875700456
chr8	124171300	124173300	2.022910283
chr8	125071100	125073100	1.758224807
chr8	126416300	126418300	2.893308617
chr9	3025700	3027700	1.878770349
chr9	14555500	14557500	3.324037644
chr9	20839300	20841300	1.859806279
chr9	21992300	21994300	2.211143108
chr9	43915900	43917900	3.432458069
chr9	44519900	44521900	1.500620599
chr9	46036900	46038900	2.340565835
chr9	48502300	48504300	2.092372305
chr9	50307100	50309100	2.036540688
chr9	54872100	54874100	2.821488902
chr9	56468300	56470300	3.792543779
chr9	62525300	62527300	2.732459238
chr9	69058900	69060900	1.917051727
chr9	103017300	103019300	1.693437161
chr9	106240100	106242100	1.332819126
chr9	106275500	106277500	1.673292613
chr9	106785900	106787900	2.260202734
chr9	107198700	107200700	3.549920415
chr9	108013500	108015500	1.867823663
chr9	118844500	118846500	1.650545931
chr9	119449900	119451900	1.498479665
chr9	119874900	119876900	1.475914773
chr9	121686900	121688900	2.589099982
chrX	5045100	5047100	4.551326536
chrX	8469500	8471500	2.868130612
chrX	57657300	57659300	2.283572591
chrX	58144500	58146500	2.412107554
chrX	58962500	58964500	2.520257944
chrX	70232300	70234300	1.791571791
chrX	108010500	108012500	1.720018705
chrX	133526300	133528300	2.037563982
chrX	138157500	138159500	2.125397932
chrX	138740100	138742100	4.384412395

### Hypometl TET1 KO hypomethylated DMRs

Chr	Start	End	False discovery rate (-log10(p-value))
chr10	12809900	12811900	3.167825

chr10	126962500	126964500	1.659
chr11	5906500	5908500	5.323866667
chr11	63332100	63334100	2.310866667
chr11	79042900	79044900	1.6131
chr11	88054100	88056100	1.4694
chr11	105026500	105028500	2.079466667
chr11	108930100	108932100	1.903266667
chr14	104996500	104998500	1.948733333
chr14	106410500	106412500	2.123866667
chr14	118840700	118842700	1.692933333
chr14	118927700	118929700	2.3837
chr15	99931100	99933100	2.238333333
chr16	89896300	89898300	1.572533333
chr16	90687100	90689100	2.118075
chr17	35201100	35203100	1.757166667
chr17	46582100	46584100	1.5647
chr19	53422500	53424500	1.944966667
chr19	56103900	56105900	1.726933333
chr19	57431700	57433700	1.698766667
chr1	37744100	37746100	1.9837
chr1	173468700	173470700	1.8541
chr1	181870500	181872500	3.1926
chr2	31680100	31682100	1.444033333
chr2	37631700	37633700	1.585733333
chr2	165653900	165655900	1.618633333
chr2	170583100	170585100	1.549233333
chr2	174120900	174122900	2.932466667
chr2	174123500	174125500	2.781433333
chr3	55156500	55158500	2.0418
chr3	83579100	83581100	2.178633333
chr3	130602900	130604900	1.531633333
chr4	42885900	42887900	1.3933
chr4	119932300	119934300	2.923166667
chr5	64309900	64311900	1.543666667
chr5	89359500	89361500	1.923766667
chr5	111056500	111058500	2.257033333
chr5	122854900	122856900	1.922566667
chr6	21969300	21971300	1.821466667
chr6	30688100	30690100	3.371366667
chr6	51118900	51120900	3.0181
chr7	56432500	56434500	1.8445
chr7	77492700	77494700	2.0156
chr7	112707700	112709700	1.426866667
chr7	149766500	149768500	2.6104

chr8	23617900	23619900	1.422933333
chr8	88047500	88049500	1.608133333
chr8	124859700	124861700	1.66682
chr9	102202900	102204900	2.730933333
chrX	33868900	33870900	2.082433333
chrX	34442900	34444900	2.045966667
chrX	45561700	45563700	1.773866667
chrX	45638500	45640500	2.8188
chrX	50097700	50099700	1.898966667
chrX	55283300	55285300	2.384966667
chrX	57800500	57802500	1.6509
chrX	58144700	58146700	1.594233333
chrX	68808700	68810700	2.17354
chrX	71211500	71213500	2.374233333
chrX	91367300	91369300	3.80544
chrX	96085500	96087500	2.043133333
chrX	96132100	96134100	1.90404
chrX	96331300	96333300	2.646625
chrX	99446700	99448700	1.874075
chrX	100676700	100678700	2.923666667
chrX	102958700	102960700	2.598733333
chrX	120216900	120218900	5.083633333
chrX	147481500	147483500	2.1876
chrX	165111700	165113700	1.4661
chrX	166415900	166417900	1.649233333
chrX	166428300	166430300	2.564066667
chrX	166434900	166436900	3.774566667