**RNA sequencing data processing**

RNAseq data was processed with the nf-core RNAseq pipeline 78 v1.2. Default parameters were used unless mentioned otherwise. Sequences were aligned to the mouse reference genome mm10 by application of the software HISAT2, with *-unstranded* option. For single-end data the *-singleEnd* option was applied. Transcripts were assembled using StringTie and gene code gene annotation release M20 79. Gene counts were generated with Stringties prepDE.py script (setting: -eb).

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**Enrichment of gene regulatory regions**

The R package LOLA was used for testing overlap and enrichment of DMRs and DARs with multi-cell gene regulatory regions from Ensembl 87,88. DMRs and DARs with an FDR < 0.05 were stratified in hypo- and hypermethylated as well as increased and decreased accessibility in *Scnn1b*-Tg vs WT AMs, respectively. Enrichment was performed against a random background for DMRs or against the common peak set identified with DiffBind for DARs 82.

Cell culture and treatment.

RAJI (ACC-319, DSMZ), MEC1 (ACC-497, DSMZ), HL60 (ACC-3, DSMZ), K562 (ACC-10, DSMZ), NCI-H1299 (CRL-5803, ATCC) cells were grown in RPMI 1640 supplemented with 10% FCS. T89G human glioblastoma cells (CRL-1690, ATCC) were kept in DMEM containing 10% FCS. Cell line authenticity and purity was confirmed using the Multiplex Cell Authentication and Cell Contamination Test by Multiplexion. Cells were treated with 500-nM (250 nM for HL60) DAC, 500-nM SB939, 1500-nM SAHA, or 500-nM (250 nM for HL60) DAC + 500-nM SB939 for 72, 18, 18, or 72 + 18 h, respectively, and compound-containing media was refreshed every 24 h.

RNA-sequencing analysis.

RNA-seq data was obtained from the Gene Expression Omnibus under accession [GSE54912](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE54912) and from the European Nucleotide Archive under accession [PRJEB5049](http://www.ebi.ac.uk/ena/data/view/PRJEB5049). Illumina and ABI\_SOLID reads were aligned against the human hg19 reference genome using HISAT version 0.1.6.-beta with default parameters and bowtie version 1.0.0 with the parameters -C,–best, respectively. Overlap of aligned reads with TE subfamilies was counted using the summarizeOverlaps function of the GenomicAlignments R/Bioconductor package[56](https://www.nature.com/articles/ng.3889#ref-CR56) with default parameters. Read counts were normalized in edgeR[57](https://www.nature.com/articles/ng.3889#ref-CR57), using the total number of uniquely mapped reads as library size. After estimation of the dispersion, statistical significance was assessed by genewise exact tests for differences in the means between two groups of negative-binomially distributed counts.

### Analysis of transposable elements.

The TINAT TE enrichment was computed based on Xie *et al*.[15](https://www.nature.com/articles/ng.3889#ref-CR15). Briefly, the enrichment score is the ratio between the observed and the expected number of transposable elements overlapping TINATs, assuming a genome-wide random distribution model. TINAT start positions in each LTR12C copy were aligned to relative locations on the LTR12C consensus sequence and the LTR12C TSS frequency was defined as the accumulated density. *De novo* motif analysis was performed using HOMER[50](https://www.nature.com/articles/ng.3889#ref-CR50) on 640 LTR12Cs that fulfilled the following two criteria: (1) No CAGE signal (CTSS tags) in DMSO control and (2) TINAT expression in both CAGE-seq replicates after DAC+SB treatment. 304 LTR12C copies without any CAGE-seq signal (CTSS tags) before and after treatment were used as a background. EMBOSS Needle tool[63](https://www.nature.com/articles/ng.3889#ref-CR63) was used to calculate the pairwise alignment between each LTR12C copy and the consensus sequence. The frequency of conserved 10mer DNA sequence in both LTR12C groups was calculated, and the sequence divergence was defined as the difference of 10mer sequence frequency between both groups.