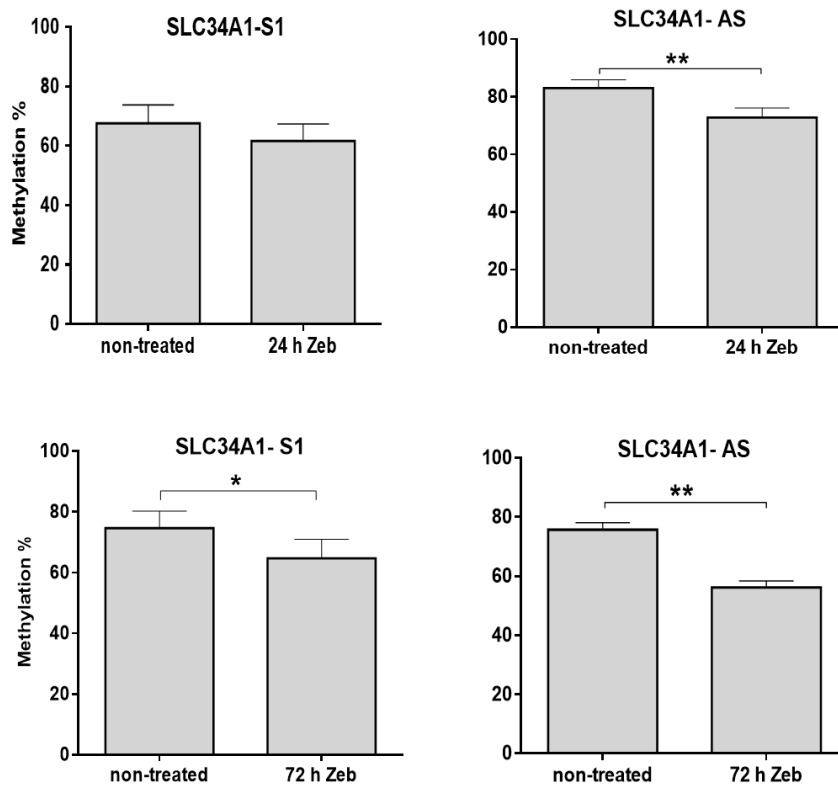
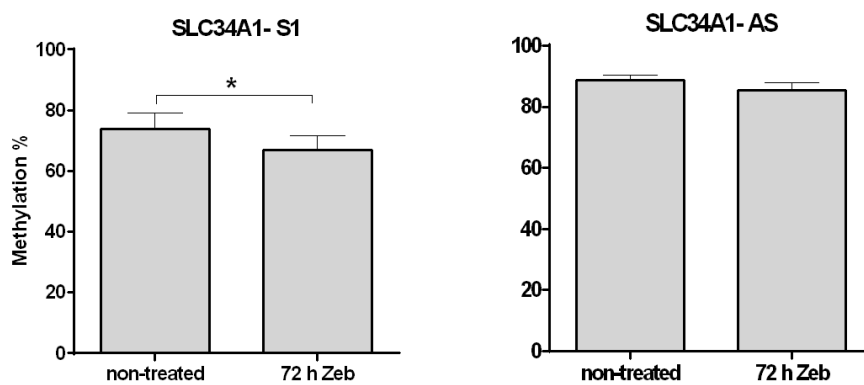


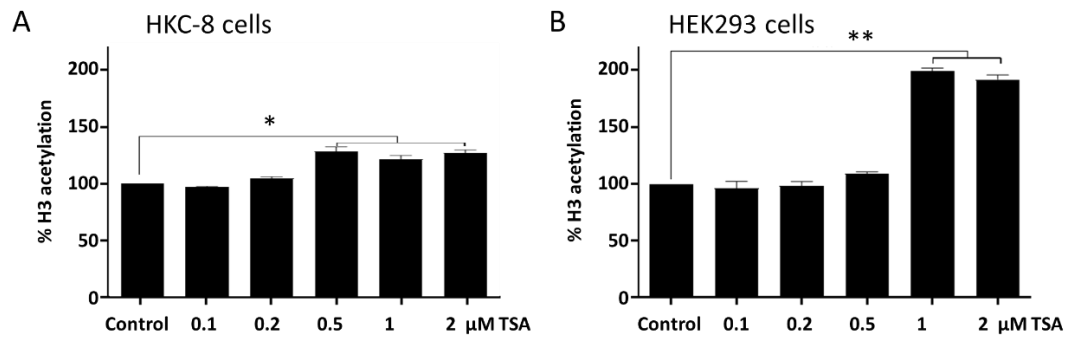
A) DNA methylation in HKC-8 cells



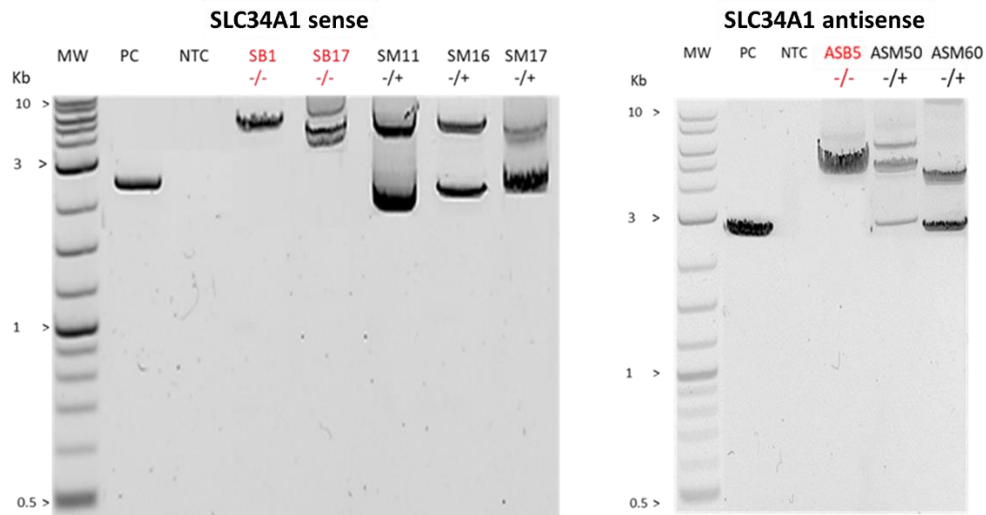
B) DNA methylation in HEK293 cells



Supplementary Figure S1: DNA methylation analysis of SLC34A1-sense (S1, S2) and SLC34A1-antisense (AS) promoters. A) HKC8 cells treated for 24 and 72 h with 50 μ M zebularine. B) HEK293 cells treated for 72 h with 50 μ M zebularine. Statistical analysis for comparing the treated cells with the control was performed by unpaired students t-test, (* = $p < 0.05$ and ** = $p < 0.01$).



Supplementary Figure S2: Global histone H3 acetylation. Histone H3 were purified and acetylation was quantified using a total histone H3 acetylation detection kit (EpiGentik). (A) HKC-8 and (B) HEK293 cells show a dose-dependent response to TSA. The data were normalised to control cells (non-treated) and treatment conditions were compared by One-Way ANOVA test using Tukey's test (* $p < 0.05$, ** $p < 0.01$).



Supplementary Figure S3: PCR analysis of CRISPR edited HEK293 clones. Clones were isolated by serial dilution in puromycin containing selection medium and genomic DNA was isolated followed by end-point PCR. For the SLC34A1 sense transcript, the expected amplicon is 2222 bp or 4112 bp with the integrated cassette. Similarly, the SLC34A1-antisense derived amplicon is 2425 bp and 4315 bp with HDR cassette. Agarose gel of PCR products including a positive control, PC (unedited HEK293) and a negative control, NTC (PCR without addition of no DNA). Sense bi-allelic (SB) clones SB1 and SB17 show bi-allelic integration (-/-, red), three clonal cells show mono-allelic integration (-/+). C) SLC34A1-antisense clone ASB5 with bi-allelic insertion (-/-, red), ASM50 and ASM60 with mono-allelic insertion (-/+).

Supplementary Table S1: Primer sequences and product length for RT-qPCR of SLC34A1 sense/antisense and GAPDH.

Oligo ID	Sequence (5'-3')	Amplicon (bp)
SLC34A1-F	CAGCCCTCAGGTCCTACACA	163
SLC34A1-R	CTCTGGCTTCTGCTCCTCCT	
SLC34A1-AS-F	TGGGCGACTGGAAGGTCTACA	182
SLC34A1-AS-R	GTCTTCGGCACCACCACAATTA	
GAPDH-F	TGAAGGTCGGAGTCAACGGATTTG	128
GAPDH-R	CATGTAAACCATGTAGTTGAGGTC	

Supplementary Table S2: Pyrosequencing primers. All primers were designed using MethPrimer webtools and synthesised by IDT, UK.

Oligo ID	Orientation	Sequence (5'-3')	bp	No. of CpG
AS1	F	TTTGTAGGAAGGTGTGTTTGT	173	3
AS1-(bio)	R	CTAAAAAATCTACATCAATACAA TAC		
AS1	SP	TTTGTAGGAAGGTGTGTTTGT		
AS1	Sequencing entry	C/TGGTTTC/TGTGAGTAC/TGTTT ATTTTTTGC/TGGC/TGAGATGGT C/TGTTAGTAGGTT		
AS2	F	GTATTGTATTGATGTAGATTTTTT AG	461	5
AS2- biotin	R	CCTAAACAACATAATAAACCTC ATCTC		
AS2	SP	TTGTGAGGTAGGTTGGG		
AS2	Sequencing entry	C/TGGGGTTGTGAC/TGTTATATA AGGC/TGTC/TG		
SLC34A1- S1-	F	AGTGGGAGTAAATTTTTATGGAG GT	339	7
SLC34A1- S1biotin	R	CATCCCAACAACTAAAATCAAA A		
SLC34A1- S1-	SP	AGTGGGAGTAAATTTTTATGGAG GT		
SLC34A1- S1-	Sequencing entry	C/TGTTTTTTTTAGTGTTTTC/TGC /TGGAGATTC/TGTTTTTTTAGTGT TTTC/TGC/TGGAGGTTTC/TGTTTT TTAG		
SLC34A1- S2-	F	TATAGGATGTTTGGGTTATTTTTT G	148	2
SLC34A1- S2biotin	R	CTATAATCAAATTCTTCCCATCA AC		
SLC34A1- S2-	SP	GTTTTTGTTTGTAGG		
SLC34A1- S2-	Sequencing entry	C/TGGGGGATGTGTTTGGGTC/T GTGGTTG		

Supplementary Table S3: Primers for ChIP-qPCR and product length. Amplicons cover the SLC34A1-sense and -antisense promoters and an SLC34A1-sense internal enhancer (i.e. SLC34A1-B).

Oligo ID	Sequence (5'-3')	Amplicon (bp)
SLC34A1-A-F3	GCCATAGGATGTTTGGGTCA	167
SLC34A1-A-R3	AGCTCTGCATGGGGAATCTA	
SLC34A1-B-F2	GTGTTTGTGCGTGTGAGTCT	193
SLC34A1-B-R2	CCACTATGAGGTCTGCAGGT	
AS-SLC34A1-F3	TATAGGATCGTGTGCGCTGCA	193
AS-SLC34A1-R3	ACGCCTGTAATCTCGTCACT	

Supplementary Table S4: Oligonucleotide sequences used for the T7-endonuclease test.

Oligo ID	Sequence (5'-3')	Oligo ID	Sequence (5'-3')
pSp-R	TAGGGGGCGTACTTG GCATATG		
S-g-1F	GTGAGGGTGTGTGGG CATGAGT	AS-T7E1234 F	CTCTAAATTCACCCAC CTCAG
S-g-1R	GAGCAGACGAAG AGGTAGAG	AS-T7E1234 F+	CAGCCACACATCACTC CTTCCTG
S-g-2F	CTCTACCTCTTCGTC TGCTC	AS-TE71234 R	CATCAGGGTGTTCAGG CTGGAG
S-g-2R	CAG CCT TACTGG GGTCACGCT	AS-TE71234 R+	CTAGGGACTCCGCAG CTGAG
S-T7E1R	CAGGGGCAGGTGTG CTCAGC	AS-T7E5678 F	CTCAAAATCCCGGCTC CACCAG
S-T7E123 F+	CAAGCCTCTGGTTCG GAGC	AS-T7E5678 F+	CAAGTGGAGGAGGAG CCAGC
S-T7E123 F++	CTGGGCGTCCTCAGT TCTC	AS-T7E5678 R	CATGCGGACAACAGCT GCGTG
S-T7E123 R+	GTCCAGGGAGCAGAC GAAGAG	AS-T7E5678 R+	GAAGGTCTACATCAGT GCAGTG
S-T7E123 F	CTGGGCTAGAGCTCA ATAATAC	AS-T7E1234 F	CTCTAAATTCACCCAC CTCAG
S-T7E23 R	GTGTAGGACTAGGGA GGGAG	AS-T7E1234 F+	CAGCCACACATCACTC CTTCCTG

Supplementary Table S5: Primers used to generate the HDR template. Lowercase letters show the overlapping region with adjacent fragments. S and AS refers to SLC34A1-sense and-antisense transcripts, respectively.

Oligo ID	Sequence (5'-3')
S-PCR1-F	CACCGCGCCCCATATAACATGTC
S-PCR1-R	CAATGCCCTGGCCTACGGATTC
S-PCR2-F	CAACTCTTCACACCCCTACAAC
S-PCR2-R	caaatgtaacgcgtctcatagGACAACATCCTGGGCACCCAC
S-PCR3-F	gttacattttgctcacgtctcgctACTACGGAGAGAGGCTGGGG TCCCCTGCTG
S-PCR3-R	cattttgctcacgtctcgctacTACGGAGAGAGGCTGGGGTTC
S-PCR4-F	gtgggtgcccaggatgttgTCCTATGAGACGCGTTACATTTG
S-PCR4-R	gaccccagcctctctccgtagTAGCGAGACGTGAGCAAAATG
AS-PCR1-F	GAGTTCCTCCCTCTAGTCCAG
AS-PCR1-R	CTGGGCAACATAGTGAGACCTC
AS-PCR2-F	CAGCACCATCTCCCCTCAAAGAC
AS-PCR2-R	gtaacgcgtctcatagggggGCATCCTCAACAAGAC
AS-PCR3-F	tgttgaggatgccccccTATGAGACGCGTTACATTTG
AS-PCR3-R	gacgcggcgtagcattagCGAGACGTGAGCAAAATG
AS-PCR4-F	ctcacgtctcgctaATGTACGCCGCGTCGG
AS-PCR4-R	CTCGCTCTGTGGCTCAGGCT

Supplementary Table S6: SLC34A1-sense/antisense genotyping PCR primers and amplicon length.

Oligo ID	Sequence (5'-3')	Amplicon (Knock-in)	Amplicon (control)
Sense-F	CACCGCGCCCCATATAACATGTC	4112	2222
Sense-R	CAATGCCCTGGCCTACGGATTC		
Antisense-F	CATGGGACTTCCTGCCTCGCTG	4315	2425
Antisense-R	CATCGTGGGCCATGCGGACA		