

Table S1. Tissue specimen information

Number	Gender	Age	Subtype	TNM stage	Location
1	male	36	protruded	T4N0M0	rectum
2	male	73	others	T3N0M0	others
3	male	64	ulcerative	T4N2M0	rectum
4	female	56	protruded	T4N1M0	rectum
5	male	52	discoid	T4N1M0	rectum
6	male	53	ulcerative	T3N0M0	rectum
7	male	78	ulcerative	T3N0M0	rectum
8	male	60	others	TisNOMO	rectum
9	male	52	ulcerative	T4N2M0	rectum
10	male	57	ulcerative	T3N2M1	colon
11	female	66	discoid	T2N0M0	rectum
12	male	47	ulcerative	T4N1M0	colon
13	male	66	discoid	T4N0M0	rectum
14	female	52	protruded	T3N0M0	colon
15	male	60	discoid	T4N0M0	rectum
16	male	64	protruded	T4N1M0	colon
17	male	69	protruded	T3N1M0	colon
18	female	61	protruded	T4N1M0	rectum
19	male	64	discoid	T4N1M0	others
20	female	79	ulcerative	T4N1M0	rectum
21	female	62	discoid	T2N0M0	rectum
22	female	61	discoid	T4N1M0	rectum
23	male	44	protruded	T3N0M0	colon
24	female	68	discoid	T4N2M1	rectum
25	male	60	discoid	T4N0M0	rectum
26	female	51	protruded	T4N2M0	rectum
27	female	45	ulcerative	T4N1M0	colon
28	female	44	protruded	T2N0M0	rectum
29	female	72	discoid	T2N0M0	rectum
30	female	52	ulcerative	T4N0M0	others
31	male	45	ulcerative	T4N2M0	rectum
32	female	53	discoid	T3N1M1	rectum
33	female	80	discoid	T4N0M0	colon
34	male	45	discoid	T4N0M0	colon
35	male	81	protruded	T2N1M0	rectum
36	male	52	discoid	T4N0M0	colon
37	female	73	discoid	T4N0M0	colon
38	male	63	discoid	T4N0M1	colon
39	female	63	ulcerative	T4N2M1	rectum
40	male	60	ulcerative	T4N1M0	rectum

41	male	58	ulcerative	T2N2M0	others
42	male	58	protruded	T2N1M0	rectum
43	female	53	ulcerative	T4N2M1	rectum
44	male	69	protruded	T3N0M0	colon

Table S2. Primers used in this study

Application	Primer	5'-3'
RT-qPCR	<i>PPIB</i>	TGTGGTGTTTGGCAAAGTTC
		GTTTATCCCGGCTGTCTGTC
	<i>CNT2</i>	AAGTAGAGCCTGAGGGAAGCAA
		GCCCAGTCCATCCCC
	<i>CNT3</i>	GAGCTGTGCAAAGCAGGGA
		TGGCGAATCCTGCTCAACTGTG
	<i>OCTN1</i>	TGCTGCTGCCACTGTTTGCT
		TTCAGGAATGAACCACCACA
	<i>MRP1</i>	TCTGGTCAGCCCAACTCTCT
		TCCTCCTCTCCAGCTGAATTA
	<i>MRP2</i>	TGTGCTCTCCTCCAGACTT
		CTGCTTCTGACCCCCACTAA
	<i>MDR1</i>	AGCTGCTGTCTGGGCAA
		TGCCAAGACCTCTTCAGCTAC
	<i>MCT1</i>	CACCGTACAGCAACTATACG
		CAATGGTCGCCTCTTGTA
	<i>MATE2K</i>	TGGGGCATATTTTACCAATG
		GAACTCCGCCATAGACACAAC
	<i>OATP1B1</i>	GAATGCCCAAGAGATGATGCTT
		AACCCAGTGCAAGTGATTTCAAT
	<i>OATP2B1</i>	GAGTTTCACCCATTCCACGTACA
		GCCACAGGACTCCATGCCT
	<i>OCT1</i>	TAATGGACCACATCGCTCAA
		AGCCCCTGATAGAGCACAGA
	<i>BCRP</i>	TCTGGC ATTTGTTTCCTC
		CTCCTGGCCCTCTACTCT
	<i>ENT1</i>	GCAAAGGAGAGGAGCCAAGA
		TTCATTGGTGGGCTGAGAGTT
	<i>ENT2</i>	CCCTGGATCTTGACCTGGAG
		GGTTTTCCCTGGCTTCTGGG
	<i>OAT10</i>	TGTGTA CTCTGCCGAGCTTTT
		CACAAGTGGTGTGAGGATGC
	<i>PEPT1</i>	TCCACCGCCATCTACCATAC
		GGACAAACACAATCAGGGCT

	<i>HDAC1</i>	ACGAAGACGACCCTGACAAG
		TCCTCACAGGCAATTCGTTT
	<i>HDAC2</i>	ATAAAGCCACTGCCGAAGAA
		TCCTCCAGCCCAATTAACAG
	<i>HDAC3</i>	ACGTGGGCAACTTCCACTAC
		GACTCTTGGTGAAGCCTTGC
	<i>HDAC4</i>	AAGAACAAGGAGAAGGGCAAG
		TGGAGAACTCTGGTCAAGGGA
	<i>HDAC5</i>	ATGTCAGGTCGGGAACCATC
		GGAAGTGGGCATGGCTCTT
	<i>HDAC6</i>	AGTCTTATGGATGGCTATTGCATG
		TGGACCAGTTAGAGGCCTTCAGG
	<i>HDAC7</i>	CCATGACGACGGCAACTTCTT
		TGCTGCGTCATGTATCCAAAAC
	<i>HDAC8</i>	AAGAGGGCGATGATGATC
		GTGGCTGGGCAGTCATAACC
	<i>HDAC9</i>	AGTGTGAGACGCAGACGCTTAG
		TTTGCTGTGCATTTGTTCTTT
	<i>HDAC10</i>	TTACTTCTCCTGGCACCGCTA
		CCACGTAGTCAGCGTTTCCC
<i>OATPIA2</i>	AATTTGAGTAATAGCACACGA	
	AATTTGAGTAATAGCACACGA	
<i>GAPDH</i>	AGGTGAAGGTCGGAGTCA	
	GGTCATTGATGGCAACAA	
ChIP-qPCR	<i>CNT2-CH1</i>	ACATACCAAATAATCTAAGCCAGAATC
		CACCACAATATTATTAGGCAATCAA
	<i>CNT2-CH2</i>	CACCTCCAGAGGCTCAAGG
		CACACGACTGTGGTTCCAGT
	<i>CNT2-CH3</i>	TCCTCACTGATCTGTTTCGTTTTT
		CGTTTTCCGTGTGAGGACAT
BSP	<i>CNT2</i>	ATGTTTATAGGAATGTATTTGTTAGAAG
		ACAAACCTAAAACCTTATACAAAATAAC

Table S3. upB formulation (pH 7.2-pH 7.4)

Ingredients	Amount
NaCl	7.3 g
D-Glucose	1.1 g
KCl	0.36 g
MgSO ₄ · 7H ₂ O	0.3 g
KH ₂ PO ₄	0.16 g
CaCl ₂	0.13 g

HEPES	6 g
ddH2O	Up to 1 L

Table S4. siRNA used in this study

Name	5'-3'
HDAC1-siRNA	CCGGUCAUGUCCAAAGUAA
HDAC2-siRNA	CUACGACGGUGAUAUUGGA
HDAC3-siRNA	AAAGCGAUGUGGAGAUUUA
HDAC4-siRNA	GCAAGAUCUCAUCGUGGA
HDAC5-siRNA	ACACGUUCAUGCUAAAGCA
HDAC6-siRNA	CCGUGAGAGUCCAACUUU
HDAC7-siRNA1	UCACUGACCUCGCCUCAA
HDAC7-siRNA2	GCACGUGAUGUACAUGCAA
HDAC8-siRNA	GGACGGUACUACAGUGUAA
HDAC9-siRNA	GAAAGACACUCCAACUAAU
HDAC10-siRNA	GGUGAACAGUGGUAUAGCA
NC	UUCUCCGAACGUGUCACGU

Disease Summary for SLC28A2

Analysis Type by Cancer	Cancer vs. Normal
Bladder Cancer	
Brain and CNS Cancer	
Breast Cancer	
Cervical Cancer	
Colorectal Cancer	5
Esophageal Cancer	1
Gastric Cancer	2
Head and Neck Cancer	
Kidney Cancer	1
Leukemia	
Liver Cancer	
Lung Cancer	
Lymphoma	
Melanoma	
Myeloma	
Other Cancer	
Ovarian Cancer	
Pancreatic Cancer	
Prostate Cancer	
Sarcoma	1
Significant Unique Analyses	1
Total Unique Analyses	9
	369

Figure S1

Summary of *CNT2* expression in various human cancers compared with normal tissues in OncoPrint™. Blue: downregulated in cancer; red: upregulated in cancer.

mRNA expression
relative to *PP1B*

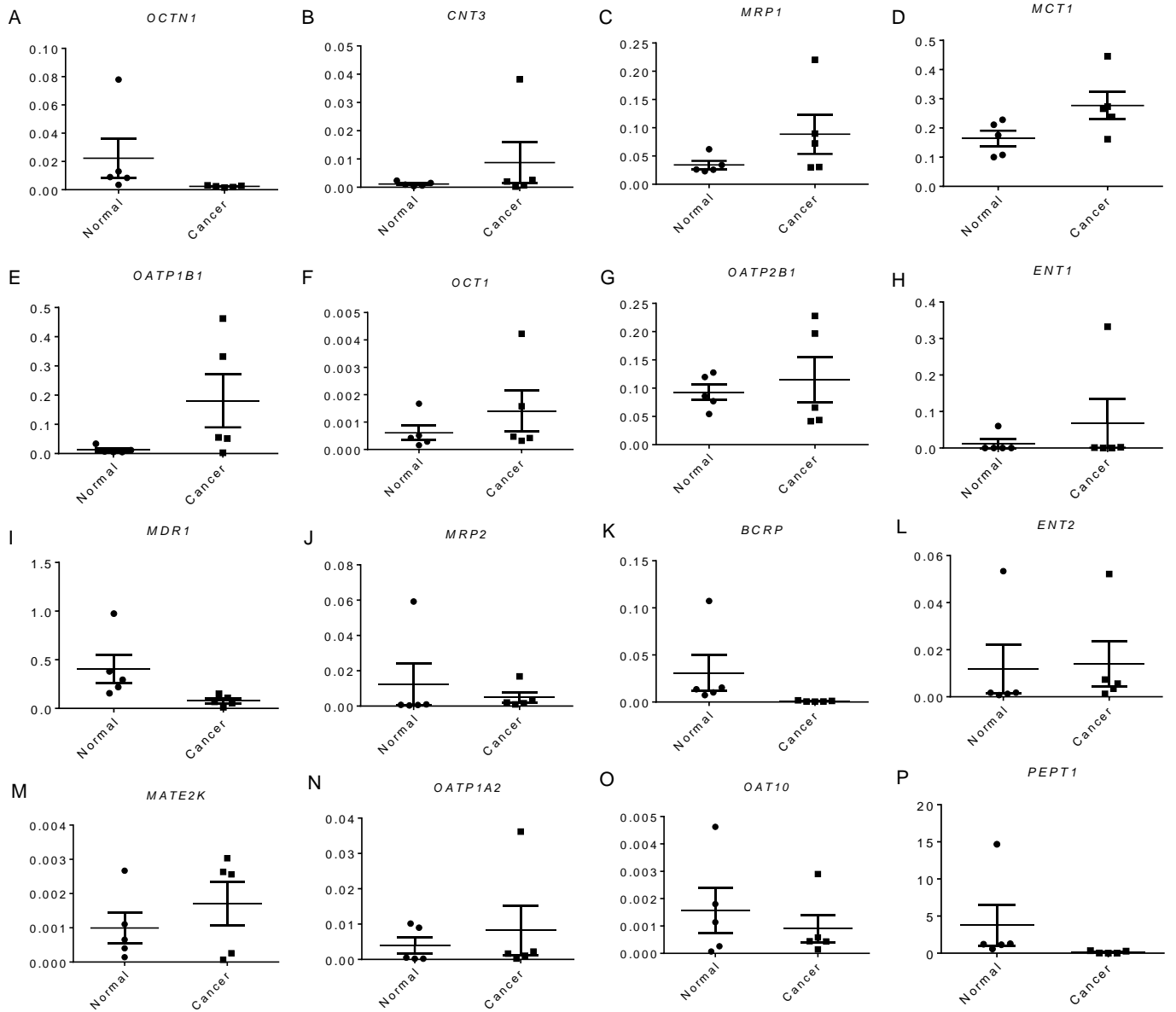


Figure S2

RT-qPCR analysis of transporters in matched CRC tissues and adjacent normal tissues normalized to reference gene *PP1B*. Results are expressed as mean \pm SEM. Two-tailed paired *t* test was used for the analysis. (A) mRNA expression of *OCTN1* in CRC (n=5). (B) mRNA expression of *CNT3* in CRC (n=5). (C) mRNA expression of *MRP1* in CRC (n=5). (D) mRNA expression of *MCT1* in CRC (n=5). (E) mRNA expression of *OATP1B1* in CRC (n=5). (F) mRNA expression of *OCT1* in CRC (n=5). (G) mRNA expression of *OATP2B1* in CRC (n=5). (H) mRNA expression of *ENT1* in CRC (n=5). (I) mRNA expression of *MDR1* in CRC (n=5). (J) mRNA expression of *MRP2* in CRC (n=5). (K) mRNA expression of *BCRP* in CRC (n=5). (L) mRNA expression of *ENT2* in CRC (n=5). (M) mRNA expression of *MATE2K* in CRC (n=5). (N) mRNA expression of *OATP1A2* in CRC (n=5). (O) mRNA expression of *OAT10* in CRC (n=5). (P) mRNA expression of *PEPT1* in CRC (n=5).

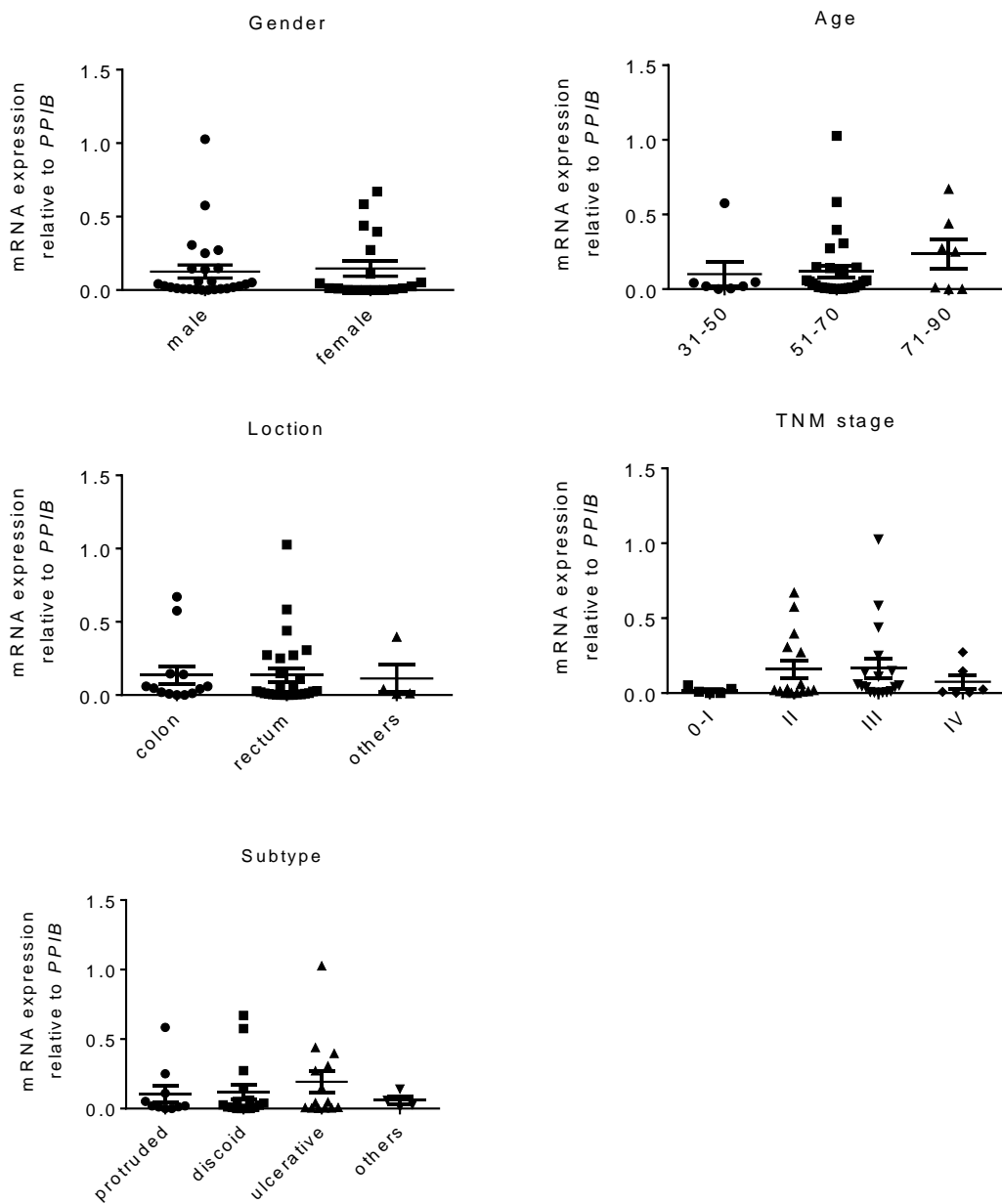


Figure S3

Relationship between CNT2 gene expression changes and gender/ age/ location/ TNM stage/ subtype in matched CRC tissues and adjacent normal tissues (n=44). Two-tailed paired *t* test was used for the analysis.

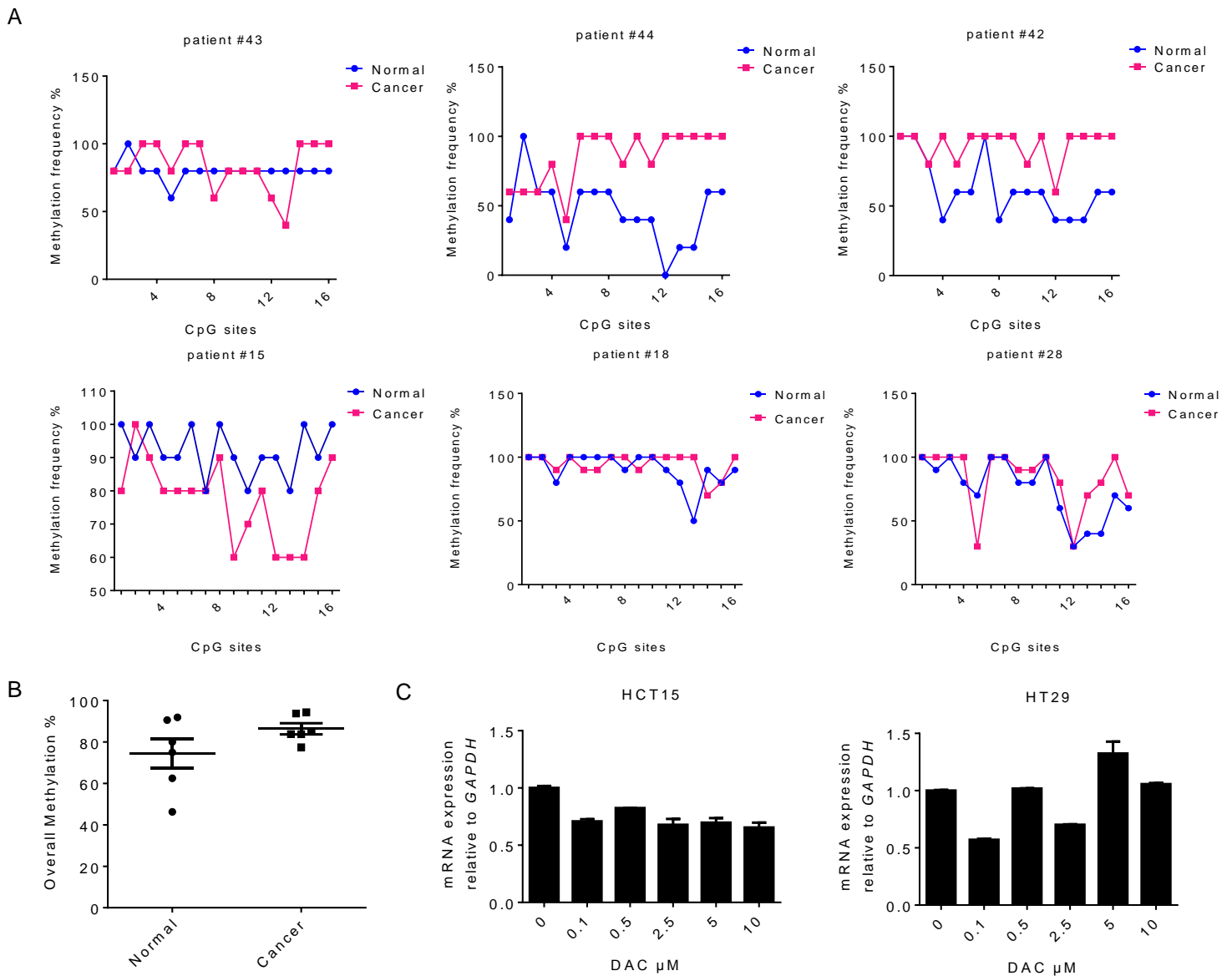


Figure S4

DNA methylation has no effect on *CNT2* expression in CRC. (A) Methylation analysis of *CNT2* promoter in human CRC tumors compared with paired adjacent normal tissues. Methylation frequency of each CpG site indicates the proportion of methylated CpG from 5 sequenced clones for patient #42, #43, #44 and 10 sequenced clones for patient #15, #18, #28. X axis represents individual CpG site 1-16. Sample number is shown at the top of each graph. (B) Overall methylation frequency in adjacent normal and cancerous CRC samples from (A), two-tailed paired *t* test was used to evaluate the difference in methylation frequency between normal and cancerous samples. (C) The expression of *CNT2* normalized to *GAPDH* in HCT15 and HT29 after treated with DAC for 72 h.

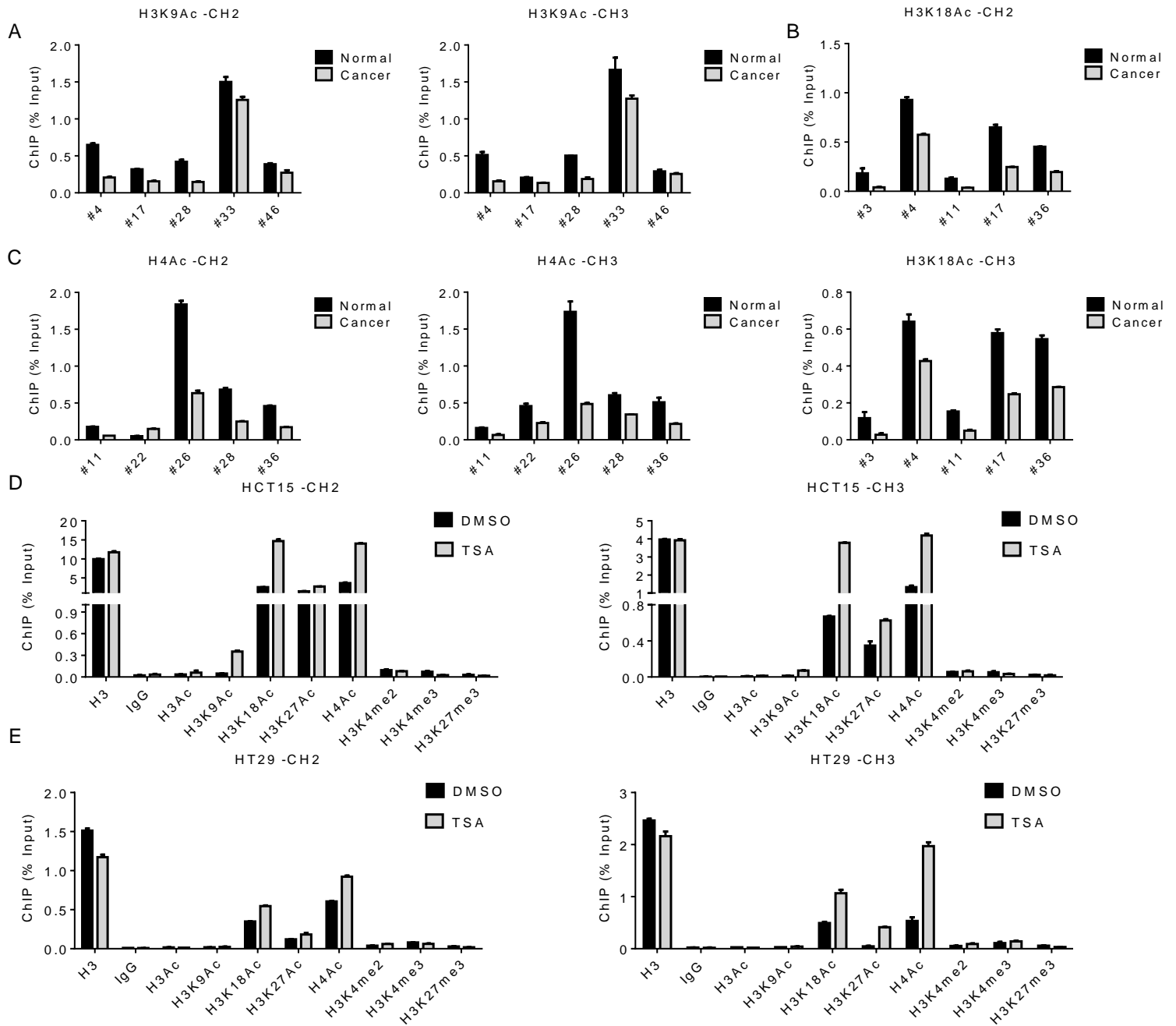


Figure S5

Histone hypoacetylation represses *CNT2* in CRC. (A) ChIP-qPCR analysis of H3K9Ac in *CNT2* promoter region in human CRC tumors compared with paired adjacent normal tissues, bar plots, mean \pm SEM. CH2, CH3 represents different primers that cover different part of *CNT2* promoter region. (B) ChIP-qPCR analysis of H3K18Ac in *CNT2* promoter region in human CRC tumors compared with paired adjacent normal tissues, bar plots, mean \pm SEM. CH2, CH3 represents different primers that cover different part of *CNT2* promoter region. (C) ChIP-qPCR analysis of H4Ac in *CNT2* promoter region in human CRC tumors compared with paired adjacent normal tissues, bar plots, mean \pm SEM. CH2, CH3 represents different primers that cover different part of *CNT2* promoter region. (D) 1 μ M TSA treatment in CRC cell line HCT15 reorganized histone modification profile at *CNT2* promoter region. (E) 1 μ M TSA treatment in CRC cell line HT29 reorganized histone modification profile at *CNT2* promoter region.

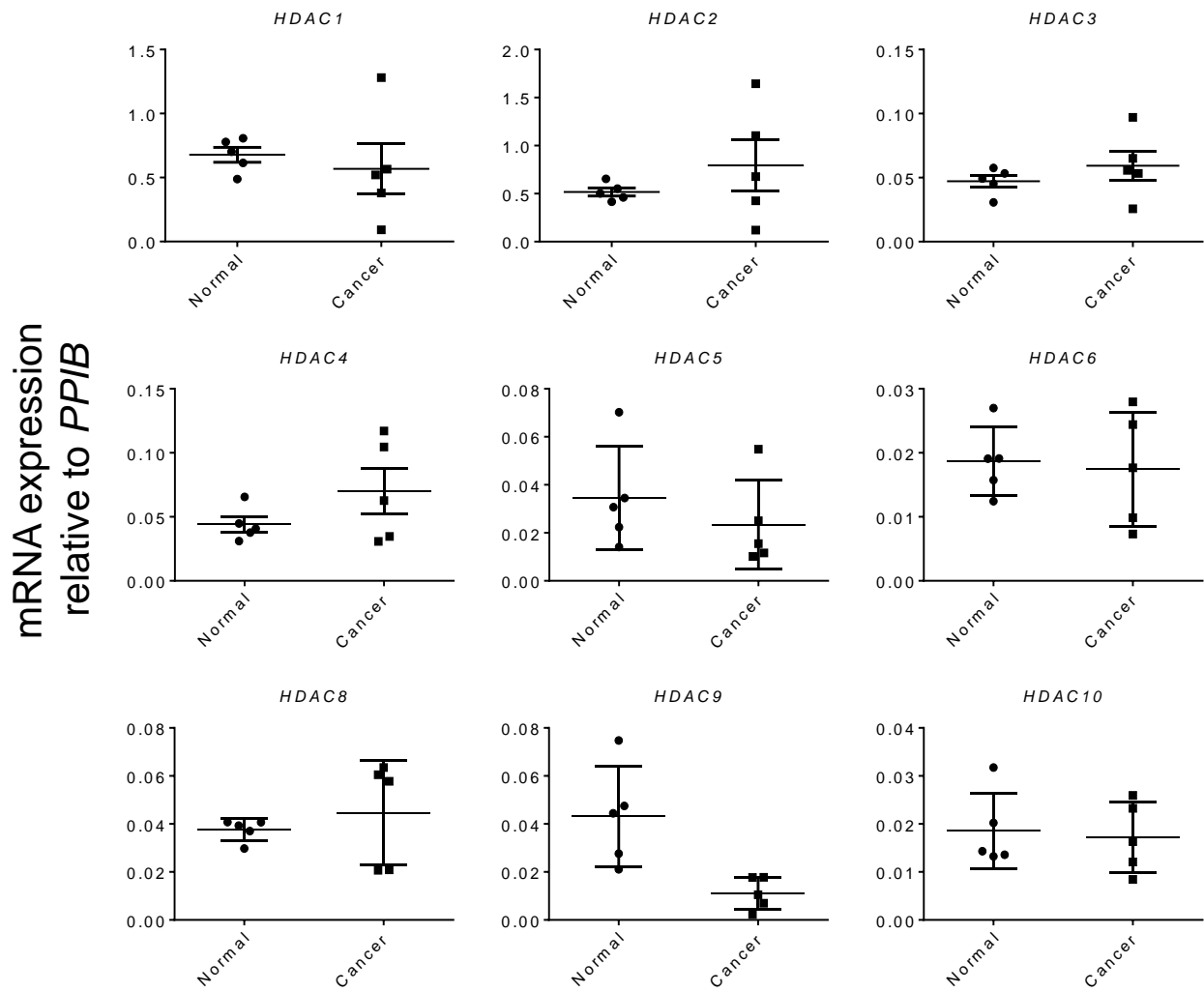


Figure S6

HDACs expression in matched CRC tissues and adjacent normal tissues (n=5). Results are expressed as mean \pm SEM. Two-tailed paired *t* test was used for the analysis.

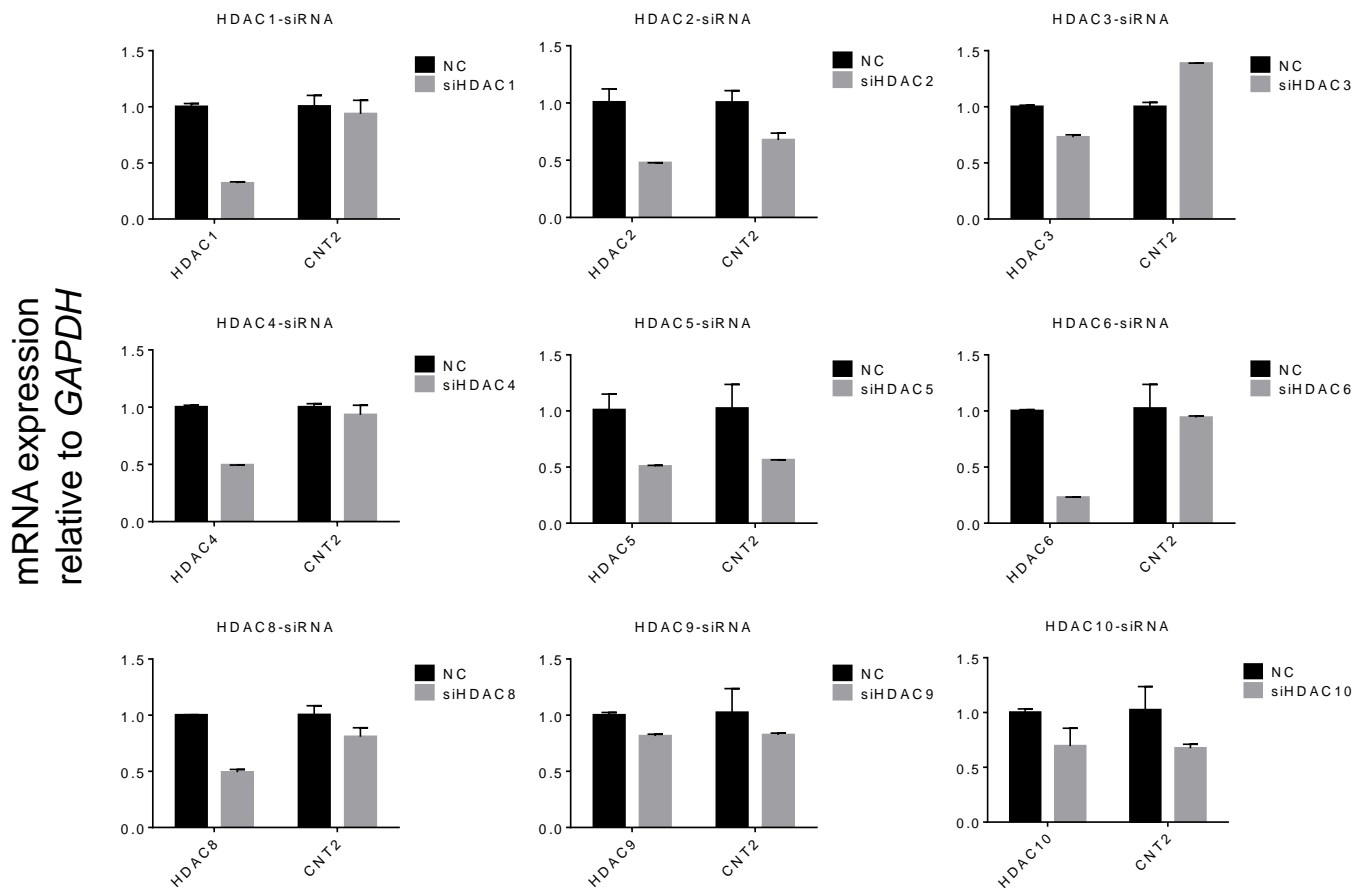


Figure S7

The expression of *CNT2* and HDACs after transfected with various siRNAs in HCT15. NC, cells transfected with negative control siRNA.

mRNA expression
relative to GAPDH

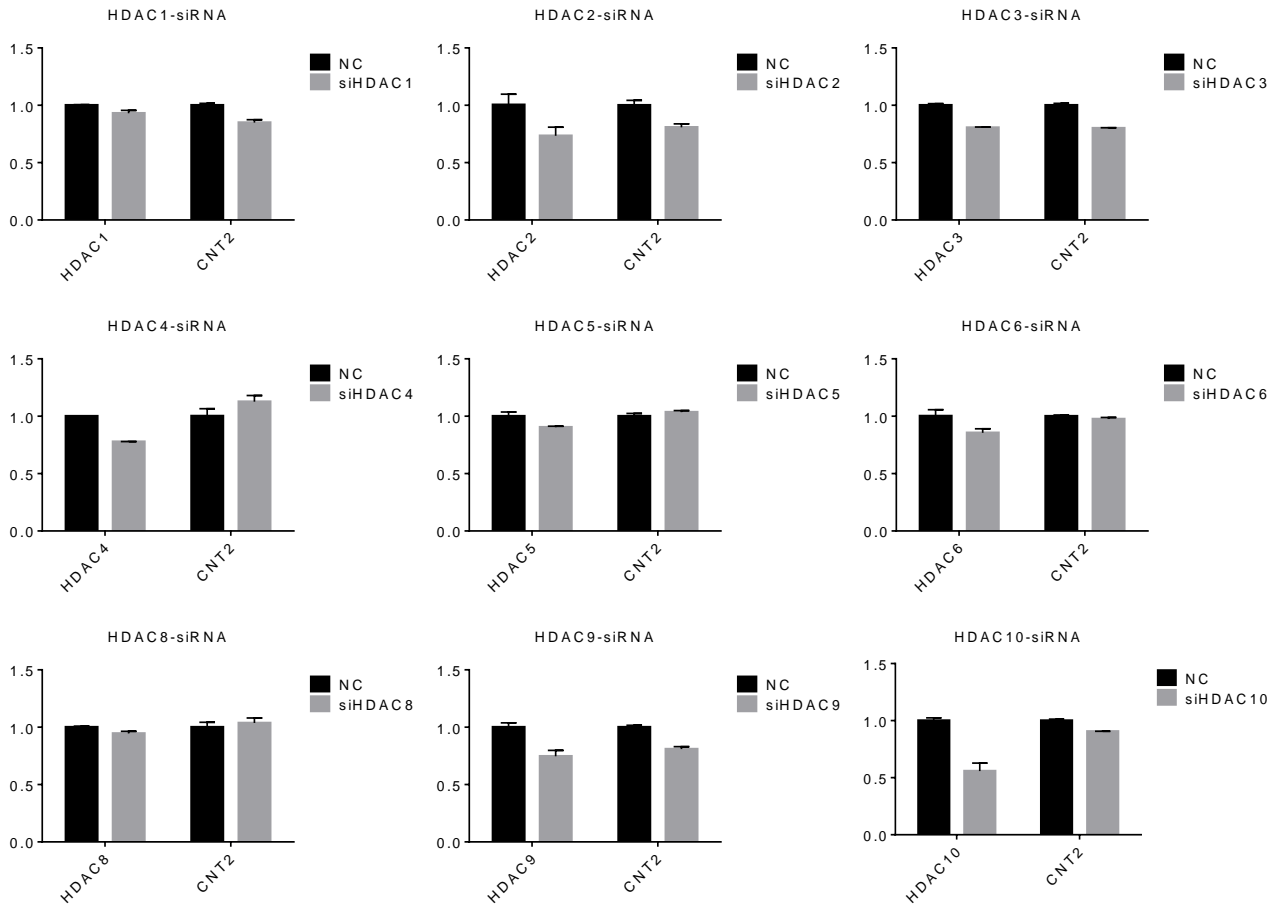


Figure S8

The expression of *CNT2* and HDACs after transfected with various siRNAs in HT29. NC, cells transfected with negative control siRNA.