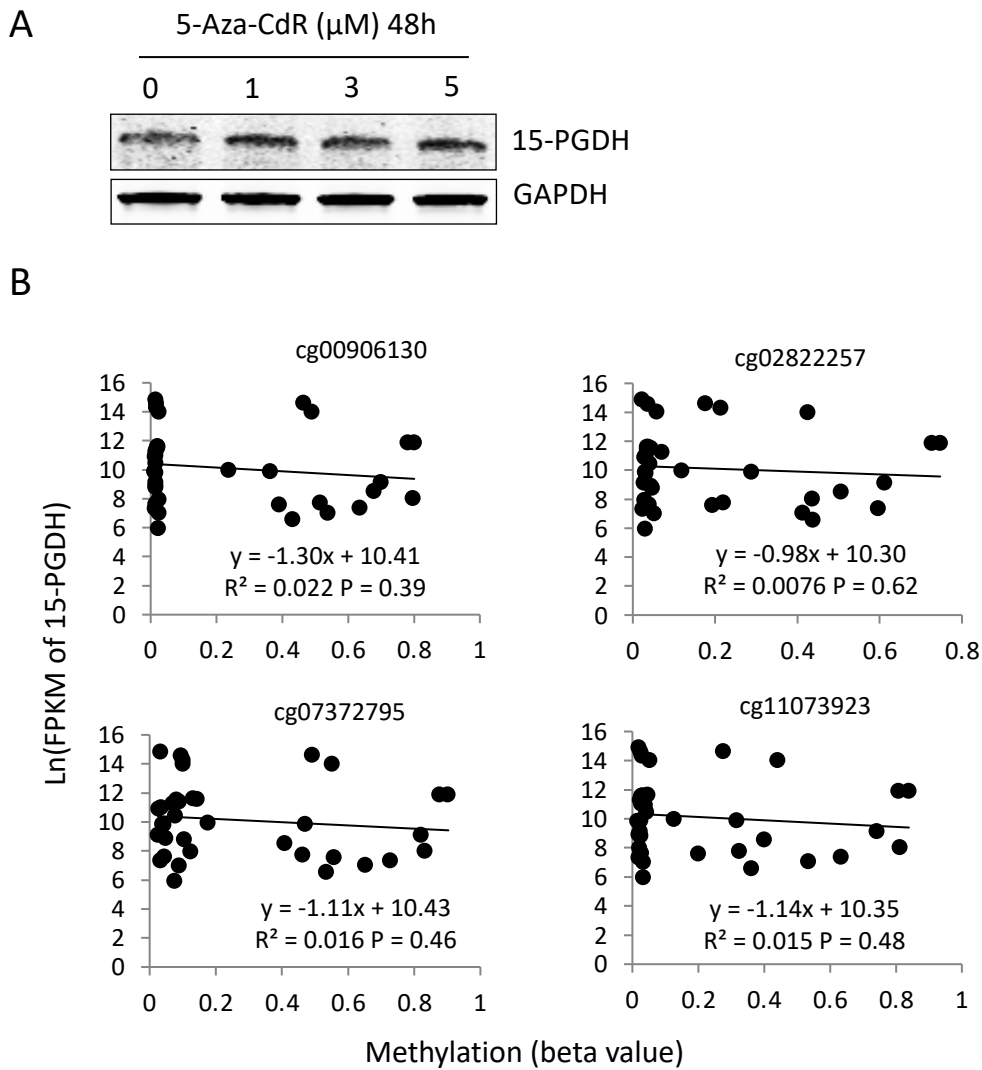


Supplementary Table 1. The mRNA levels of 53 HMTs (some HMTs are denoted by multiple probes) in 91 CCA tumor tissues and 92 non-tumor tissues from dataset GSE76297.

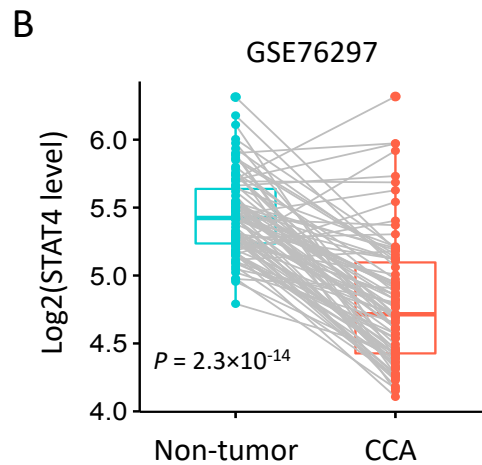
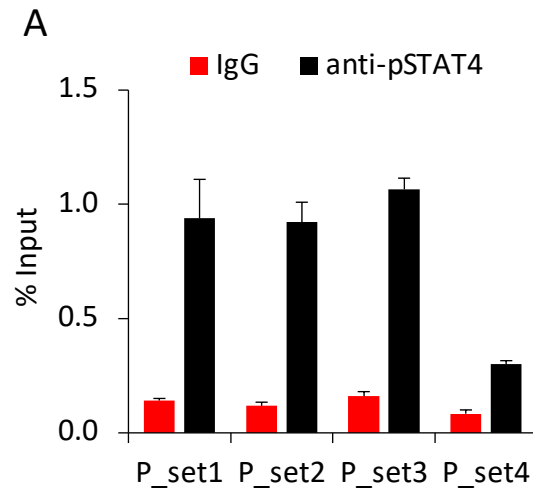
Probe ID	Gene Symbol	CCA_ASD (log2)	NT_ASD (log2)	Fold Change (C/N)	Raw p-value	Bonferroni p-value
TC07001993.hg.1	EZH2	6.22	5.14	2.1	0	0
TC06000844.hg.1	PRDM1	6.34	5.43	1.9	0	0
TC11002900.hg.1	KMT2A	8.88	8.06	1.8	0	0
TC07000679.hg.1	KMT2E	8.40	7.59	1.8	0	0
TC19002199.hg.1	PRMT1	8.14	7.31	1.8	0	0
TC04000030.hg.1	NSD2	7.00	6.26	1.7	0	0
TC08002292.hg.1	NSD3	5.00	4.20	1.7	0	0
TC11001064.hg.1	KMT2A	8.47	7.76	1.6	0	0
TC11002899.hg.1	KMT2A	7.91	7.25	1.6	0	0
TC08001145.hg.1	NSD3	7.25	6.60	1.6	0	0
TC17001540.hg.1	EZH1	7.30	6.73	1.5	0	0
TC19002646.hg.1	PRMT1	7.73	7.14	1.5	0	0
TC11000257.hg.1	PRMT3	5.54	5.00	1.5	0	0
TC10001914.hg.1	SUV39H2	4.93	4.36	1.5	0	0
TC12001928.hg.1	PRDM4	6.83	6.38	1.4	0	0
TC21000265.hg.1	PRMT2	6.44	5.96	1.4	0	0
TC14000940.hg.1	PRMT5	7.04	6.58	1.4	0	0
TC01001194.hg.1	SETDB1	6.48	6.00	1.4	0	0
TC01004054.hg.1	SMYD3	5.57	5.10	1.4	0	0
TC07002045.hg.1	KMT2C	8.48	8.12	1.3	4.18E-13	2.95E-08
TC05001011.hg.1	NSD1	7.16	6.76	1.3	0	0
TC03000038.hg.1	SETD5	7.55	7.16	1.3	0	0
TC10000113.hg.1	SUV39H2	5.14	4.82	1.3	1.78E-15	1.25E-10
TC19000188.hg.1	CARM1	7.21	6.92	1.2	2.04E-12	1.44E-07
TC06001550.hg.1	EHMT2/G9a	6.23	5.99	1.2	0	0
TC6_apd_hap1000091.hg.1	EHMT2/G9a	6.25	6.01	1.2	0	0
TC6_cox_hap2000177.hg.1	EHMT2/G9a	6.24	5.99	1.2	0	0
TC6_dbb_hap3000166.hg.1	EHMT2/G9a	6.23	5.99	1.2	0	0
TC6_mcf_hap5000152.hg.1	EHMT2/G9a	6.25	6.01	1.2	0	0
TC6_qbl_hap6000167.hg.1	EHMT2/G9a	6.24	6.00	1.2	0	0
TC6_ssto_hap7000146.hg.1	EHMT2/G9a	6.31	6.06	1.2	0	0
TC01000067.hg.1	PRDM16	6.32	6.03	1.2	1.13E-11	7.97E-07
TC13000198.hg.1	SETDB2	5.42	5.22	1.2	8.01E-06	0.56472771
TC02000439.hg.1	SMYD5	5.61	5.33	1.2	6.88E-15	4.85E-10
TC12003277.hg.1	KMT2D	7.12	6.93	1.1	3.62E-07	0.02550309
TC12000985.hg.1	KMT5A	7.22	7.14	1.1	4.68E-05	1
TC11002004.hg.1	KMT5B	6.90	6.72	1.1	1.35E-08	0.00095376
TC05002762.hg.1	NSD1	3.67	3.59	1.1	0.00193664	1
TC21000477.hg.1	PRDM15	5.91	5.84	1.1	1.90E-05	1
TC01000182.hg.1	PRDM2	5.81	5.64	1.1	6.28E-11	4.43E-06
TC04001508.hg.1	PRDM5	3.69	3.54	1.1	6.68E-07	0.04707475
TC09000852.hg.1	EHMT1	6.78	6.77	1.0	0.71578764	1
TC11003375.hg.1	KMT2A	4.58	4.62	1.0	0.24889279	1
TC07002682.hg.1	KMT2C	4.24	4.31	1.0	0.14609472	1
TC11002449.hg.1	PRDM10	6.26	6.20	1.0	0.01170078	1
TC11000378.hg.1	PRDM11	6.51	6.55	1.0	0.02130603	1
TC11002650.hg.1	PRDM11	4.66	4.66	1.0	0.96778674	1
TC04002696.hg.1	PRDM5	2.50	2.52	1.0	0.30429905	1
TC16001364.hg.1	PRDM7	4.48	4.56	1.0	1.82E-05	1
TC01000925.hg.1	PRMT6	5.81	5.88	1.0	0.00221093	1
TC16000555.hg.1	PRMT7	6.37	6.45	1.0	0.00308077	1
TC16000364.hg.1	SETD1A	6.62	6.66	1.0	0.01012753	1
TC03001364.hg.1	SETD2	7.33	7.30	1.0	0.36772555	1
TC03000012.hg.1	SETMAR	5.64	5.65	1.0	0.76391217	1
TC03002197.hg.1	SETMAR	6.08	6.15	1.0	0.12228588	1
TC01001790.hg.1	SMYD2	6.56	6.59	1.0	0.63006753	1
TC17000984.hg.1	SMYD4	6.22	6.22	1.0	0.97073409	1
TC19000049.hg.1	DOT1L	6.62	6.73	0.9	0.00043001	1
TC19001937.hg.1	DOT1L	5.72	5.86	0.9	1.02E-06	0.07194135
TC12002349.hg.1	KMT2D	4.71	4.94	0.9	5.42E-12	3.82E-07
TC19000894.hg.1	KMT5C	6.47	6.59	0.9	1.50E-08	0.00105498
TC11000377.hg.1	PRDM11	5.04	5.14	0.9	1.37E-07	0.00966434

Probe ID	Gene Symbol	CCA_ASD (log2)	NT_ASD (log2)	Fold Change (C/N)	Raw p-value	Bonferroni p-value
TC11003140.hg.1	PRDM11	5.48	5.71	0.9	3.84E-14	2.71E-09
TC09000739.hg.1	PRDM12	5.70	5.89	0.9	3.33E-15	2.35E-10
TC06000831.hg.1	PRDM13	4.67	4.87	0.9	1.38E-14	9.71E-10
TC08001307.hg.1	PRDM14	3.92	4.13	0.9	0	0
TC04002178.hg.1	PRDM5	3.17	3.33	0.9	2.58E-11	1.82E-06
TC05000114.hg.1	PRDM9	4.44	4.62	0.9	0	0
TC12000040.hg.1	PRMT8	4.02	4.11	0.9	6.35E-06	0.44761987
TC12000963.hg.1	SETD1B	6.52	6.66	0.9	1.39E-08	0.00097956
TC14001499.hg.1	SETD3	7.17	7.32	0.9	9.20E-06	0.64882297
TC02000539.hg.1	SMYD1	3.53	3.69	0.9	0	0
TC0X000258.hg.1	SUV39H1	5.39	5.53	0.9	1.26E-11	8.91E-07
TC04001583.hg.1	SETD7	6.95	7.46	0.7	0	0

ASD: average signal density.



Supplementary Figure S1: (A) Western blots show that 5-Aza-CdR treatments have little effects on 15-PGDH level in CCLP1 cells. The cells were treated with 1, 3 or 5 μM of 5-Aza-CdR for 48 hours. **(B)** The correlation between the methylation beta values of four CpG islands in 15-PGDH gene promoter region (denoted by composite element cg00906130, cg02822257, cg07372795 and cg11073923 in Infinium Human Methylation450 BeadChip) and the 15-PGDH mRNA levels in the tumor tissues of TCGA-CHOL CCA patients (n=36).



Supplementary Figure S2: (A) ChIP analyses. DNA from formaldehyde crosslinked CCLP1 cells was sonicated into short fragments and incubated with anti-pSTAT4 or IgG. The precipitated DNA samples were analyzed by real-time PCR using 15-PGDH promoter specific primer sets schemed in Figure 5A. **(B)** STAT4 mRNA levels in 90 CCA tumor and their matched non-tumor tissues pairs from microarray dataset GSE76297.