

Supplementary information, Figure S4 Loss of 5hmC facilitates the gene body hypermethylation in tumor tissue and promotes tumorigenesis. (A) Heatmap of the 5mC levels in tumor and matched normal tissues at the 5hmC-modified sites in promoters and gene body regions, respectively. The scale bar from yellow to red represents the number of 5hmC-modified sites from low to high. (B) The heatmap of the *p* values. The scale bar from red to yellow represents the *p* value from 0 to 1. *P* value for the number of the overlapped sites between DhMS and DMS was calculated using a custom script based on BEDTools fisher. (C) Similar analysis as (A), but  $5mC_{BS}$  was estimated by BS-seq data. (D) Wiggle tracks of four representative gene loci.  $\Delta$  means the difference of 5mC or 5hmC level between ccRCC and normal samples. The red and green box highlighted two adjacent hypermethylated genes, COL6A2 and FTCD, in chromosome 21 which showed the opposite association with gene expression. (E)

The venn diagrams of the number of overlapped genes between genes with hypo-5hmC and aberrant DNA methylation in promoter or gene body regions. (F) The KEGG pathways analyses of the genes with both hypo-5hmC and hyper-5mC in gene body were shown. The significance was evaluated by P value. P1 and P2 represent patient 1 and 2, respectively.