Figure S1 | mRNA expression level of TET2 and TET3.

TET2 (a) and TET3 (b) expression level among hESCs, somatic tissues and HCCs in expression microarray (U133 plus 2.0, Affymetrix). TET2, Gene Name- KIAA1546, Probe Name: 227624at. Lower: TET3, Gene Name: hCG_40378, Probe Name: 235542at. hESC, human embryonic stem cell; HCC, hepatocellular carcinoma; LC, liver cirrhosis (corresponding non-cancerous liver); NL, normal liver.
Figure S2 | Clinicopathological characteristics of HCC patients associated with TET1 expression. Clinical characteristics of HCCs. AFP, α-fetoprotein; DCP, des-gamma-carboxy prothrombin; Data are shown as median ± quartile. p values are measured by Mann–Whitney U test. **p < 0.01; ***p <0.001.
Figure S3 | 5mC and 5hmC profiles of clinical liver tissues.
(a) Relative TET2 (upper) and TET3 (lower) mRNA expression of hepatoma cells and clinical liver samples by RT-qPCR. TET1 high HCCs, HCCs of high level TET1 (GeneChip score > 50); TET1 low HCC, HCC of low level TET1 (GeneChip score < 50). Data are shown as mean ± SD from triplicate experiments. (b) Genome-wide profiling of 5mC (upper) and 5hmC (lower) for clinical liver tissues in ACTB and GAPDH locus. (c) 5mC distributions relative to human RefSeq gene position by MeDIP-seq at different expression levels in clinical liver samples. (d) 5hmC and 5mC distributions relative to each gene position around TSS (±5kb) by hmeDIP-seq (upper) and MeDIP-seq (lower) for clinical liver samples according to their gene expression levels. Expression level, High; GeneChip score > 250, Low; GeneChip score < 25, Medium; GeneChip score 25-250.
Figure S4 | Expression level of TET1 in 807 CCLE cancer cell lines.
The 807 CCLE cancer cell lines are arranged in order of TET1 expression level and shown in a gray bar graph. The 23 liver cancer cell lines are shown in black, and their names are appended above.
CCLE: Broad Institute Cancer Cell Line Encyclopedia, https://portals.broadinstitute.org/ccle
Figure S5 | 5hmC and 5mC distributions of liver cancer cell lines.
(a) 5hmC and 5mC distributions relative to each gene position around TSS by hmeDIP-Seq (upper) and MeDIP-seq (lower) with regard to the expression levels in HepG2 and Huh7 cells. (b) 5mC distributions relative to human RefSeq gene position by MeDIP-seq according to the expression levels in HepG2 and Huh7. Expression level, High; GeneChip score > 250, Low; GeneChip score < 25, Medium; GeneChip score 25-250
Figure S6 | 5mC and 5hmC mapping of HMGA2 locus for clinical liver tissues.
5mC- (blue) and 5hmC- (red) enriched regions of HMGA2 locus are demonstrated using Integrative Genomics Viewer (IGV). The box with dotted lines indicates intragenic enhancer regions identified by ChIP-sequencing analysis of liver cancer cells.
Figure S7 | **Sanger Sequence of 3C chimeric fragments.**
The PCR product is cloned and sequenced with primers that anneal to the vector backbone.
Figure S8 | 5mC and 5hmC mapping of HMGA2 locus for clinical liver tissues. 5mC- (blue) and 5hmC- (red) enriched regions of HMGA2 locus are demonstrated using Integrative Genomics Viewer (IGV). The box with dotted lines indicates intragenic enhancer regions identified by ChIP-sequencing analysis of liver cancer cells.
Figure S9 | 5mC and 5hmC mapping of HMGA2 locus for clinical liver tissues.

5mC- (blue) and 5hmC- (red) enriched regions of HMGA2 locus are demonstrated using Integrative Genomics Viewer (IGV). The box with dotted lines indicates intragenic enhancer regions identified by ChIP-sequencing analysis of liver cancer cells.
Figure S10 | Histone modification status 5mC and 5hmC mapping of HMGA2 locus for clinical liver tissues. 5mC- (blue) and 5hmC- (red) enriched regions of HMGA2 locus are demonstrated using Integrative Genomics Viewer (IGV). The box with dotted lines indicates intragenic enhancer regions identified by ChIP-sequencing analysis of liver cancer cells.
Table S1

| Name  | Sequence                         |
|-------|----------------------------------|
| siTET1-1 | AAUCAAGCGGAAGAAUAACUCAACA       |
| siTET1-2 | GGCUACACGAUAGCUCCAUUUAU         |
| siTET1-3 | GGAAGCACUGGUUUUGUACCUCUAA       |
| siHMGA2-1 | GAACCAACCGUGAGCCUCUCCUA        |
| siHMGA2-2 | GGAACUGAAGACAUCCUCACAA         |

Table S1 | Sense sequence of siRNAs targeting *TET1* and *HMGA2*. 
| Name     | Sequence                                      |
|----------|-----------------------------------------------|
| TET1 forward | TGATGACAGAGTTCTTGACACATAAG                   |
| TET1 reverse | CAGGTGCAGCGTCTCAGTGTT                       |
| HMGA2 forward | CCCTGGCTTTGGAGTGTCCTTCTAAC                |
| HMGA2 reverse | TTCAACAAGCAAGCGATTCA                       |
| ACTB forward | AGAAGGAGATCACTGCCCTGGCACC                  |
| ACTB reverse | CCGCTTTGCTGATCCACATCTGCTG                  |

Table S2 | Primer sequence for qRT-PCR.
### Table S3

| Name          | Method   | Pass filtered reads | %PF  | Uniquely mapped reads | %Mapped |
|---------------|----------|---------------------|------|------------------------|---------|
| HepG2 H3K4me3 | ChIP-seq | 32,990,100          | 91.81% | 29,102,178             | 88.21%  |
| Huh7 H3K4me3  | ChIP-seq | 30,934,362          | 92.29% | 26,583,453             | 85.94%  |
| HepG2 H3K4me1 | ChIP-seq | 36,466,336          | 93.02% | 30,116,105             | 82.59%  |
| Huh7 H3K4me1  | ChIP-seq | 34,450,215          | 93.12% | 29,201,716             | 84.76%  |
| HepG2 H3K27ac | ChIP-seq | 37,973,262          | 91.67% | 33,063,351             | 87.07%  |
| Huh7 H3K27ac  | ChIP-seq | 34,881,946          | 92.47% | 30,167,015             | 84.76%  |
| HepG2 siCTL   | hmeDIP-seq | 27,656,345        | 80.15% | 15,458,915             | 55.90%  |
| HepG2 siTET1  | hmeDIP-seq | 23,980,711        | 76.72% | 14,563,272             | 60.73%  |
| Huh7 siCTL    | hmeDIP-seq | 26,189,474        | 85.25% | 14,596,475             | 55.73%  |
| Huh7 siTET1   | hmeDIP-seq | 24,907,605        | 85.12% | 13,199,788             | 53.00%  |
| HCC-1         | hmeDIP-seq | 37,810,304        | 67.76% | 25,894,022             | 68.48%  |
| HCC-2         | hmeDIP-seq | 35,767,631        | 77.84% | 22,767,529             | 63.65%  |
| HCC-3         | hmeDIP-seq | 35,882,246        | 75.74% | 24,785,685             | 69.08%  |
| HCC-6         | hmeDIP-seq | 22,626,199        | 82.69% | 14,352,956             | 63.44%  |
| LC-6          | hmeDIP-seq | 24,539,865        | 79.37% | 16,848,046             | 68.66%  |
| NL-1          | hmeDIP-seq | 23,633,662        | 80.51% | 14,220,659             | 60.17%  |
| HepG2 siCTL   | MeDIP-seq | 36,090,315        | 76.35% | 14,836,630             | 41.11%  |
| HepG2 siTET1  | MeDIP-seq | 36,717,093        | 78.68% | 15,832,332             | 43.12%  |
| Huh7 siCTL    | MeDIP-seq | 34,350,531        | 77.03% | 19,973,064             | 58.14%  |
| Huh7 siTET1   | MeDIP-seq | 30,282,870        | 71.81% | 18,790,623             | 62.05%  |
| HCC-1         | MeDIP-seq | 23,021,818        | 62.42% | 15,331,339             | 66.59%  |
| HCC-2         | MeDIP-seq | 24,757,221        | 77.47% | 16,987,547             | 68.62%  |
| HCC-3         | MeDIP-seq | 27,363,962        | 79.30% | 16,750,731             | 61.21%  |
| HCC-6         | MeDIP-seq | 31,374,006        | 64.62% | 20,666,264             | 65.87%  |
| LC-6          | MeDIP-seq | 32,867,789        | 68.19% | 17,932,016             | 54.56%  |
| NL-1          | MeDIP-seq | 35,991,252        | 65.15% | 14,859,379             | 41.29%  |

**Table S3 | Lists of ChIP-seq, hmeDIP-seq, and MeDIP-seq performed in this study.**
| Name            | Strand | Sequence                      |
|-----------------|--------|-------------------------------|
| HMGA2_enh1      | forward| TAGGGAAAATATTGAATTGGTTTG      |
| HMGA2_enh1      | reverse| ACACAAATAACTCTTTTCACAAAAATAC |
| HMGA2_enh2      | forward| TTTGGTGAAAGAGTTTTGTGTG       |
| HMGA2_enh2      | reverse| TTATCATTTAAAATCAACCCCTTCC     |
| HMGA2_enh3      | forward| CATACAAAACCTTACCCTCCCTC      |
| HMGA2_enh3      | reverse| TATGAAAAAGGGTGAATTTATAG      |
| HMGA2_enh4      | reverse| CTATTCTACATCCATTACAAATAC     |
| HMGA2_enh5      | forward| TATTGATTGGTAAATGGAGTGAGA     |
| HMGA2_enh5      | reverse| TAAAAACTCATTTAACCTCTTTACA    |
| HMGA2_enh6      | forward| GGTGTGAGATGATTGGGTATTG       |
| HMGA2_enh6      | reverse| CTATTCACTAACATTTTTCAACTA    |
| HMGA2_enh7      | forward| AAATTTTTTGGAGAAAATGGAATTTAGA |
| HMGA2_enh7      | reverse| ACTAAACCCTAACTAACCATAA     |
| HMGA2_enh8      | forward| GTATGTATTTGGATAATGGTG        |
| HMGA2_enh8      | reverse| TCCCTTACATCTACTAAATTTCCA    |
| HMGA2_enh9      | forward| TGAAAGGAATGTTTTAGGAGG       |
| HMGA2_enh9      | reverse| AATCCCTCTAAATATTACCTCAA    |
| HMGA2_enh10     | forward| TAACATTCAAAAAATCATC         |
| HMGA2_enh10     | reverse| TAGAAGATTTGTTTTAGAATGG       |
| HMGA2_enh11     | forward| AGAAGTAGATTTTTGGATTGTTT      |
| HMGA2_enh11     | reverse| CCAAAACTCATCTCCTAACTAC       |
| HMGA2_enh12     | forward| TGGTTGTGGATTAATGTTAGAGT      |
| HMGA2_enh12     | reverse| TAAATTTAATTAATCTCATTACCC    |
| HMGA2_enh13     | forward| TATGATTAGTTTTGATTG          |
| HMGA2_enh13     | reverse| ATCCCTCCTTAAACCTACCTCC       |
| HMGA2_enh14     | forward| GAGGATGGTGAAGAGTAATG         |
| HMGA2_enh14     | reverse| TAAATAATTTACTCTTATTACCTCAAC |
| HMGA2_enh15     | forward| GTATTTTAGTTTGATGATAAGAG      |
| HMGA2_enh15     | reverse| AATAAAAATTTAAACTATTAAACAAC   |

**Table S4 | Primer sequence for 3C-qPCR.**
Table S5 | Primer sequence for multiplex targeted sequence of BS-treated amplicons.

| Name            | Site | Sequence                      |
|-----------------|------|-------------------------------|
| Constant primer | (1)  | GTCTCCGATGTGTTTGCTCTC         |
| Test primer 2   | 2    | ATGTGCTGTTGCTATTAAGTAAG       |
| Test primer 3   | 3    | TGGCCGGTGTGATAGTG             |
| Test primer 4   | 4    | CATTCTGTAAAGCTAATTGCACAAAC    |
| Test primer 5   | 5    | GTGGTTGCTTTCTTCGGCATGTATC     |
| Test primer 6   | 6    | AGCTTTGTGATCCCTCTGGTAATG      |
| Test primer 7   | 7    | GTGCTGAAAGGATAAAGGTAATAG      |
| Test primer 8   | 8    | TGGCTCACTTCATCCACAAC          |
| TaqMan probe    |      | ACTGGTGCTAGTGTCAC             |