| Gene       | Forward (5' to 3') | Reverse (5' to 3')  |  |
|------------|--------------------|---------------------|--|
| SAMHD1     | ACTGCCATCATCTTGGAA | GGGCAAACTTAATAAAGC  |  |
|            | TCCAA              | GCTTGT              |  |
| MAP2K6     | GAAGCATTTGAACAACC  | CCTGGCTATTTACTGTGGC |  |
|            | TCAGAC             | TC                  |  |
| KLF4       | CCAGAGGAGCCCAAGCC  | ATCCACAGCCGTCCCAGT  |  |
|            | AAAG               | С                   |  |
| GAPDH      | GGGAAGGTGAAGGTCGG  | GGGGTCATTGATGGCAAC  |  |
|            | AGT                | А                   |  |
| SAMHD1-151 | CGGGGTACCCCGAAGGG  | CCCAAGCTTGGCTACACC  |  |
|            | CTCAACTGTC         | TGGCGTCCG           |  |
| SAMHD1-233 | CGGGGTACCTGGCGGGA  | CCCAAGCTTGGCTACACC  |  |
|            | TTGATTTGAG         | TGGCGTCCG           |  |
| SAMHD1-285 | CGGGGTACCTGCCCTCA  | CCCAAGCTTGGCTACACC  |  |
|            | GTTCTGCTTC         | TGGCGTCCG           |  |
| SAMHD1-399 | CGGGGTACCAGGTGCGG  | CCCAAGCTTGGCTACACC  |  |
|            | CGGGTAGTGTA        | TGGCGTCCG           |  |
| SAMHD1-553 | CGGGGTACCACTGTGGA  | CCCAAGCTTGGCTACACC  |  |
|            | ATGAAGACACCCTC     | TGGCGTCCG           |  |
| SAMHD1-667 | CGGGGTACCTGGGAATG  | CCCAAGCTTGGCTACACC  |  |
|            | CAGTTGGGATG        | TGGCGTCCG           |  |

Table S1. Sequence of primers in this study

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| SAMUDI 027   | CGGGGTACCTAAGCTATT | CCCAAGCTTGGCTACACC |  |
|--------------|--------------------|--------------------|--|
| SAMIDI 1050  | CCGCCTCAT          | TGGCGTCCG          |  |
|              | CGGGGTACCTGGAGTGC  | CCCAAGCTTGTTCTCGGG |  |
| SAMIDI-1950  | AACGGGAAGA         | CTGTCATCG          |  |
| SAMHD1-285   | CTGCTTCTAGCCACGAA  | ACGTGAACGCGAAATTTC |  |
| mutant       | ATTTCGCGTTCACGT    | GTGGCTAGAAGCAG     |  |
| SAMUD1 Chip  | GCTCTTTCCTCCCCCTTT | GCAGTCCAGTCGTCCTCA |  |
| SAWIIDI-CIII | CC                 | AA                 |  |

| Antibodies    | Company     | Cat.No     | Concentration |
|---------------|-------------|------------|---------------|
| Anti SAMUDI   | Proteintech | 12586-1-AP | WB: 1:2000    |
| Αίμι-SAΜΠDΙ   |             |            | IHC: 1:200    |
| Anti-HA-tag   | ABclonal    | AE008      | WB: 1:2000    |
| Anti-MAP2K6   | Proteintech | 12745-1-AP | WB: 1:500     |
| Anti-Phos-p38 | Affinity    | AF4001     | WB: 1:500     |
| Anti-p38      | Affinity    | AF6456     | WB: 1:500     |
| Anti-GAPDH    | Affinity    | AF7021     | WB: 1:3000    |
|               | Proteintech | 11880-1-AP | WB: 1:500     |
| Anu-KLF4      |             |            | ChIP: 2 µg    |

 Table S2. The information of primary antibodies in this study

## Fig.S1



**Fig.S1 Establishment of HGC-27 and MGC-803 cells with stable knockdown of SAMHD1**. (**a**, **b**) Western blot was used to detect the expression levels of SAMHD1 protein in HGC-27 cells. (**c**) The expression levels of SAMHD1 mRNA in HGC-27 cells were detected using qRT-PCR. (**d**, **e**) Western blot was used to detect the expression levels of SAMHD1 protein in MGC-803 cells. (**f**) The expression levels of SAMHD1 mRNA in MGC-803 cells were detected using qRT-PCR.



**Fig.S2 Establishment of AGS cells with stable overexpression of SAMHD1**. (a) Western blot was used to detect the expression levels of SAMHD1 protein in AGS cells. (b) The expression levels of SAMHD1 mRNA in AGS cells were detected using qRT-PCR.



**Fig.S3 Analysis of differentially expressed genes in AGS and HGC-27 cells. (a)** The RNA seq was performed in AGS cells from SAMHD1 and Vector groups, and the Volcano plot is presented. **(b)** The RNA seq was performed in HGC-27 cells from shRNA-1 and shNC groups, and the Volcano plot is presented. **(c)** Venn diagram of differentially expressed genes in AGS and HGC-27 cells. Each set of mapping data was obtained from two independent RNA-seq.



**Fig.S4 Identification of core promoter of SAMHD1 gene**. (a) Schematic diagram of pGL3 plasmids containing SAMHD1 promoter. (b) Double luciferase reporting assay was used to identify the core promoter of SAMHD1 gene.