



Supporting Information

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TRADES: Targeted RNA Demethylation by SunTag System

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J. Mo, S. Qin, Prof. X. Weng, Prof. X. Zhou

College of Chemistry and Molecular Sciences, Wuhan University, Wuhan 430072, China

E-mail: xcweng@whu.edu.cn; xzhou@whu.edu.cn

Z. Chen, Prof. Y. Zhou

The Institute for Advanced Studies, College of Life Sciences, State Key Laboratory of Virology, Wuhan University, Wuhan 430072, China

S. Li, C. Liu, L. Zhang, Y. Kong, Prof. X. Zhang

State Key Laboratory of Virology and Hubei Province Key Laboratory of Allergy and Immunology and Department of Immunology, School of Medicine, Wuhan University, Wuhan 430071, China.

R. Ran, Prof. S. Liu

Department of Clinical Laboratory, Center for Gene Diagnosis and Program of Clinical Laboratory, Zhongnan Hospital, Wuhan University, Wuhan, 430071, China.

Prof. F. Wang

Wuhan University School of Pharmaceutical Sciences, Wuhan, 430071, China.

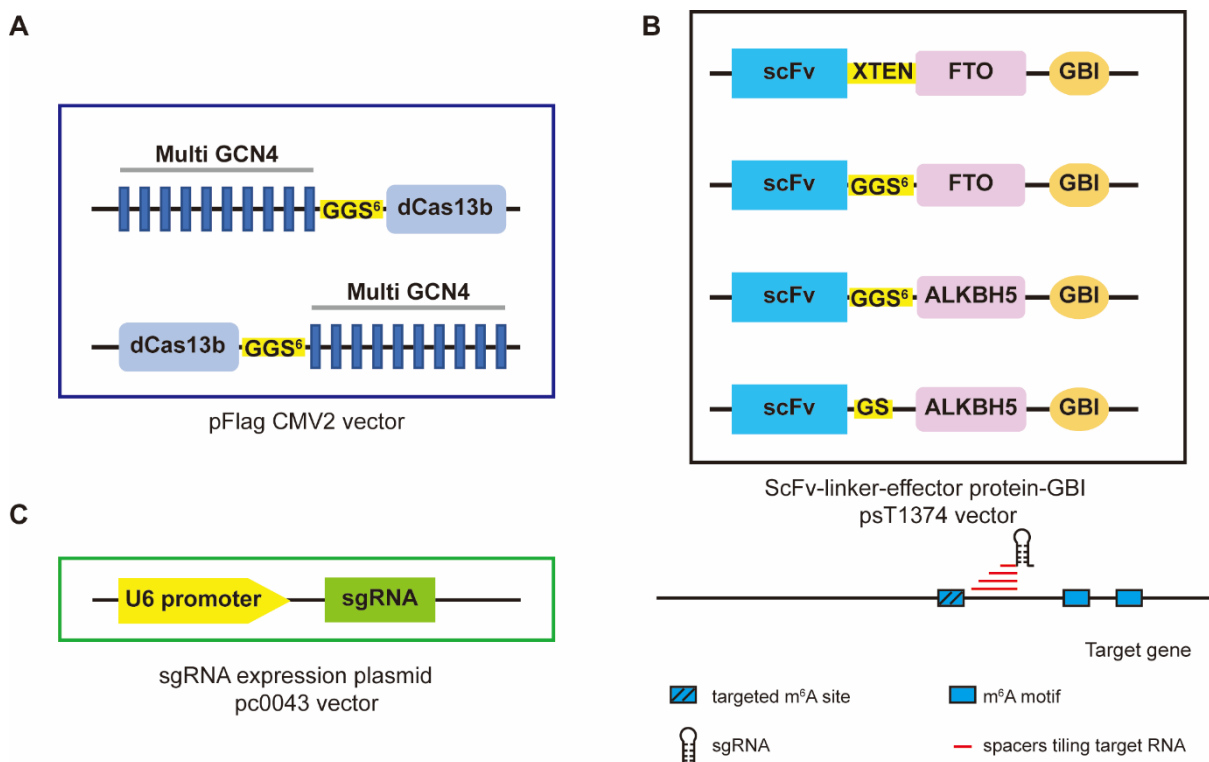


Figure S1 | The structure of plasmids used in this paper and the verification of their expression by Western-blot. (A) The schematic representation of plasmids. Multi-GCN4 peptides were inserted to the N-terminal or C-terminal of dCas13b. The vector used in this part is pFlag CMV2. (B) The schematic representation of plasmids used for demethylation. All these four kinds of plasmids have wild-type and mutant effector protein. The vector used in this part is psT1374. (C) sgRNA is the transcription product of U6 promoter in pc0043 vector. The red lines stand for the spacers tiling to the target RNA.

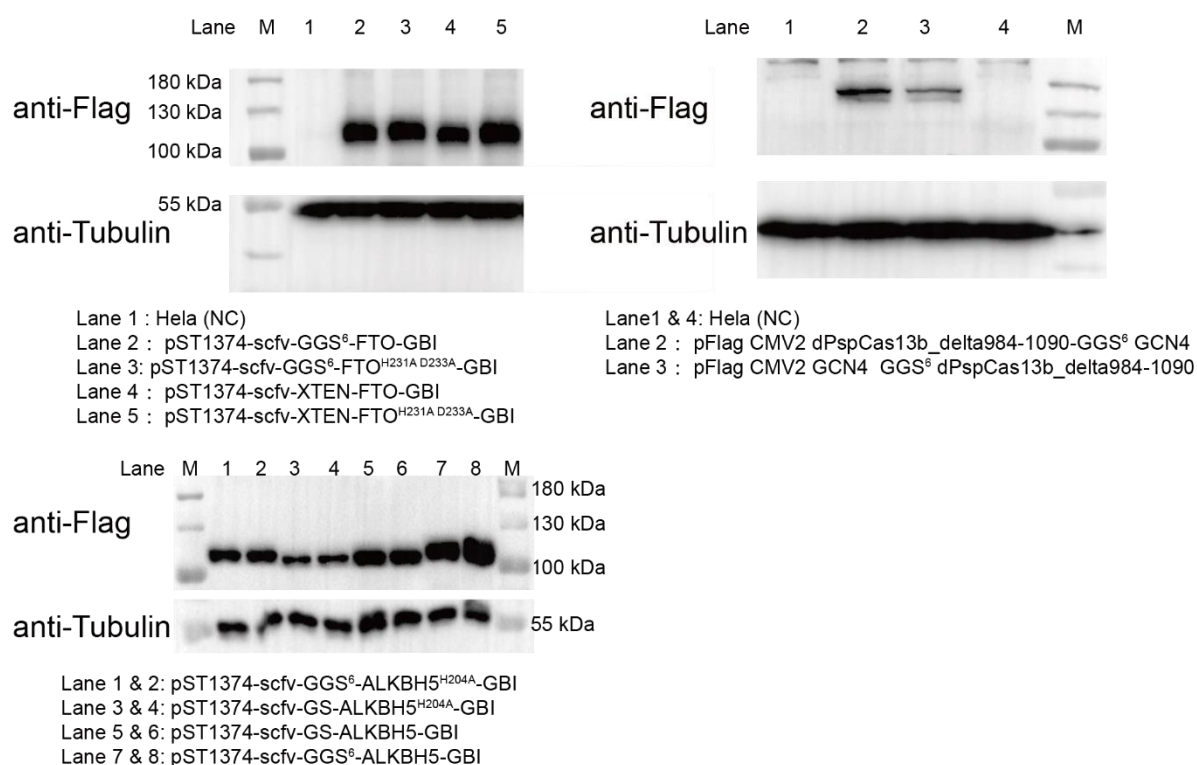


Figure S2 | The verification of recombinant protein expression by Western-blot. Protein expression of these recombinant plasmids transfected in HeLa cells. All plasmids were engineered with Flag tag. This experiment was repeated twice with similar results.

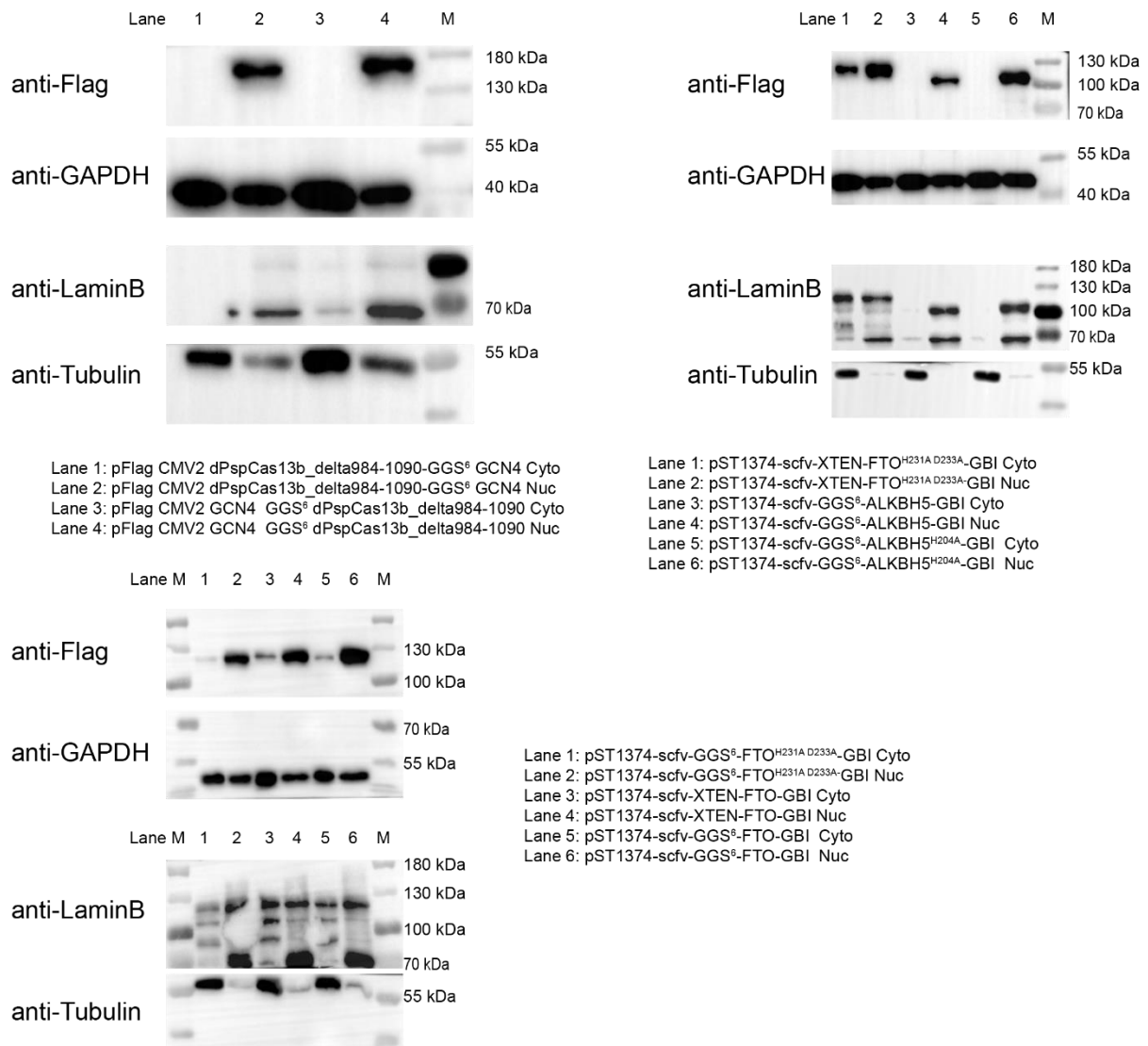


Figure S3 | Subcellular localization of these recombinant proteins in HeLa cells. Cyto means the cytoplasmic fraction of HeLa cells, Nuc means nuclear fraction of HeLa cells. The high expressions of these proteins in Nuc indicated that nuclear localization of these recombinant proteins. This experiment was repeated twice with similar results.

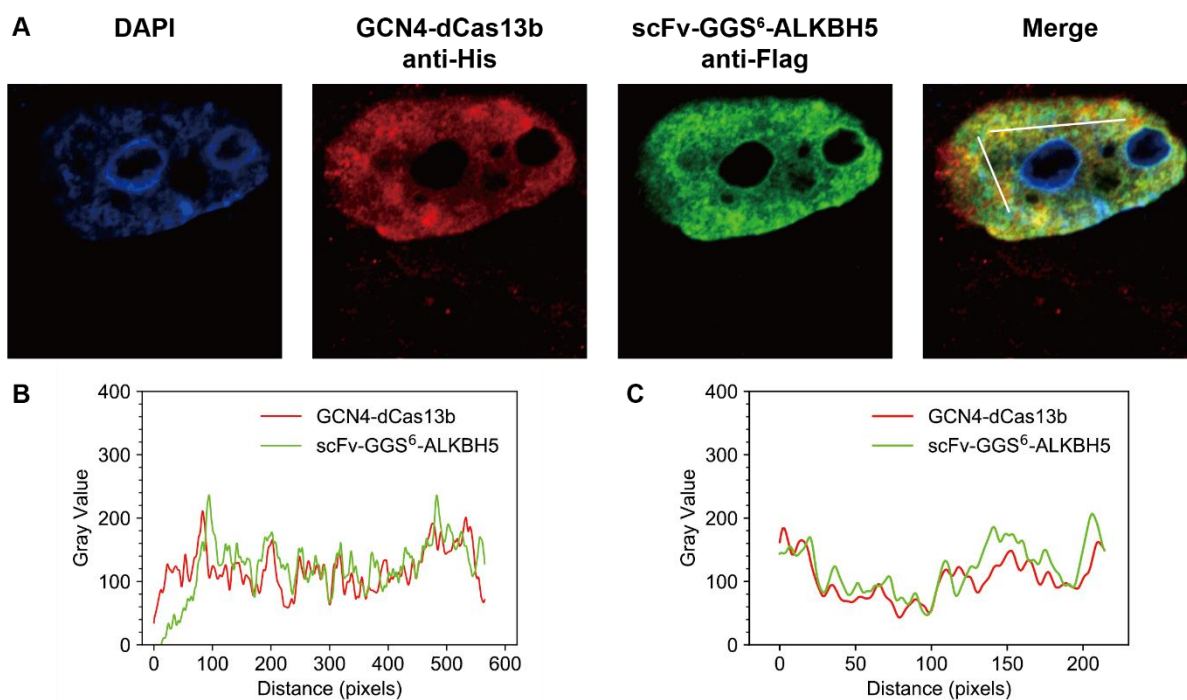


Figure S4 | The co-localization of dCas13b and RNA m⁶A demethylase by immunofluorescence staining. (A) GCN4-dCas13b, scFv-GGS⁶-ALKBH5 were co-expressed in HeLa cells for overall 48 hours. Then cells were imaged using confocal microscopy. The GCN4-dCas13b plasmid was engineered with His-tag, while the scFv-GGS⁶-ALKBH5 was engineered with Flag-tag. (B) Profile plots of gray value of GCN4-dCas13b (red) and scFv-GGS⁶-ALKBH5 (green) corresponding to the region marked with white lines in Figure S4A (merge).

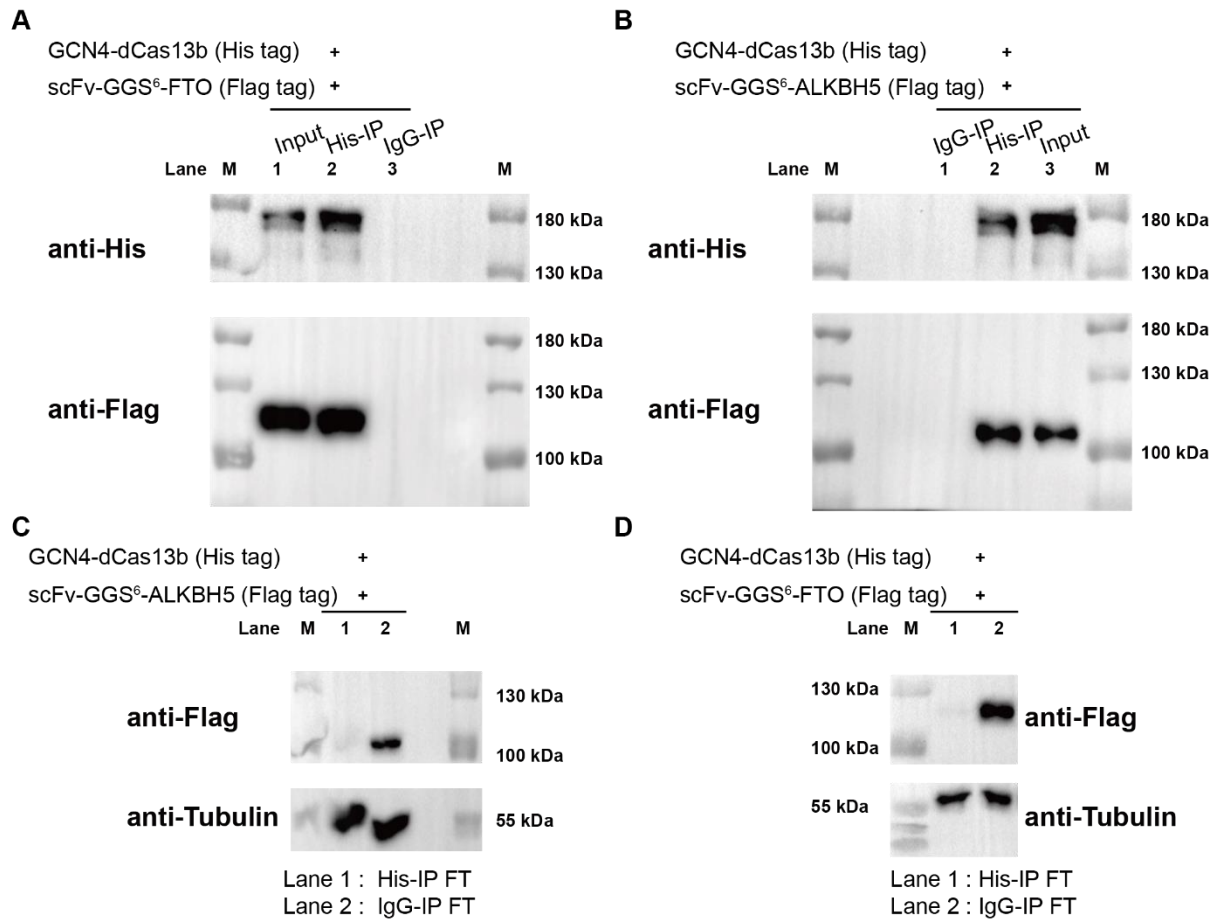


Figure S5 | GCN4-dCas13b could capture scFv-GGS⁶-effector proteins in transfected cells.

(A) Co-immunoprecipitation of the GCN4-dCas13b-interacting protein scFv-GGS⁶-FTO. Western blot using the indicated antibodies with IgG used as control for the immunoprecipitation. (B) Co-immunoprecipitation of the GCN4-dCas13b-interacting protein scFv-GGS⁶-ALKBH5. Western blot using the indicated antibodies with IgG used as control for the immunoprecipitation. (C) Flow through of Co-IP experiment shown in A. (D) Flow through of Co-IP experiment shown in B. These experiments were repeated four times with similar results.

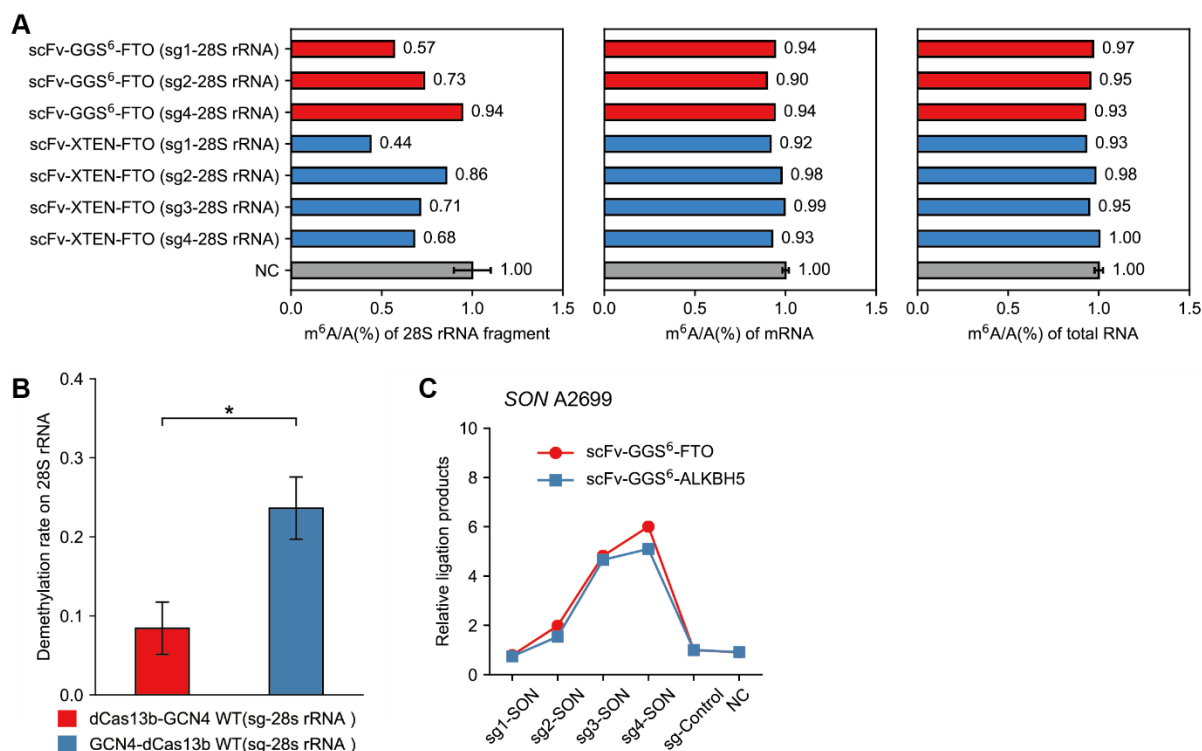


Figure S6 | Screen of sgRNA for 28S rRNA and SON. (A) m⁶A/A (%) of 28S rRNA fragment, mRNA and total RNA in individual groups were quantified by LC-MS/MS. All groups excepted negative control (NC) were transfected with GCN4-dCas13b. ScFv-GGS⁶-FTO or scFv-XTEN-FTO and sgRNA were transfected as indicated. For NC, bars represent mean \pm SD from two independent experiments. (B) The demethylation rate on 28S rRNA fragment in individual groups were quantified by LC-MS/MS. All groups were transfected with scFv-XTEN-FTO and sg1-28S rRNA. GCN4-dCas13b or dCas13b-GCN4 was transfected as indicated. Bars represent mean \pm SD from two independent experiments (n = 2, two-tailed Student's t-test). (C) Measurement of m⁶A level on SON A2699 in individual groups. Relative ligation products of each group were quantified by qPCR. Cells excepted NC group were all transfected with GCN4-dCas13b. ScFv-effector proteins and sgRNA were transfected as indicated for overall 48 hours. NC stands for negative control.

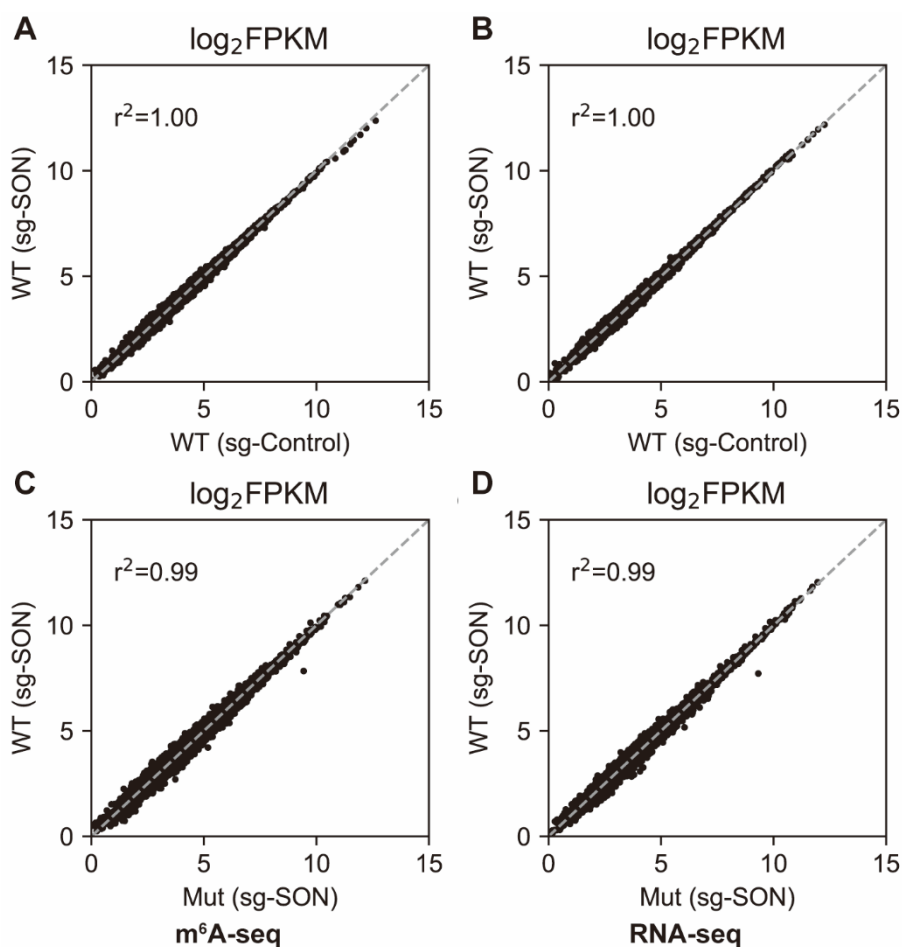


Figure S8 | TRADES performs good on-target capability. (A) Pearson correlation of RPKM between m⁶A-enriched mRNA samples treated as indicate. **(B)** Pearson correlation of RPKM between input mRNA samples treated as indicate. **(C)** Pearson correlation of RPKM between m⁶A-enriched mRNA samples treated as indicate. **(D)** Pearson correlation of RPKM between input mRNA samples treated as indicate.

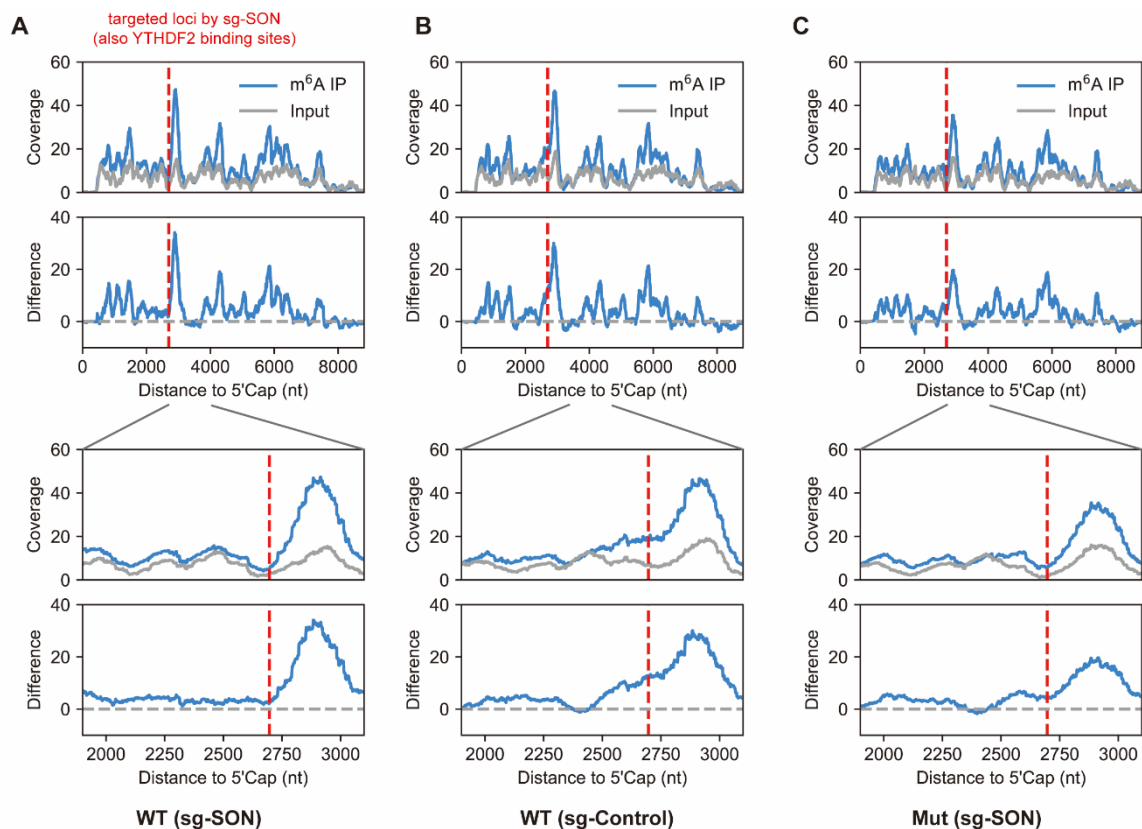


Figure S9 | TRADES performs good demethylation effect on SON A2699. (A) Comparison of normalized read coverages of SON mRNA between input mRNA and m⁶A-enriched mRNA which are both from WT (sg-SON) treated samples. (B) Comparison of normalized read coverages of SON mRNA between input mRNA and m⁶A-enriched mRNA which are both from WT (sg-Control) treated samples. (C) Comparison of normalized read coverages of SON mRNA between input mRNA and m⁶A-enriched mRNA which are both from Mut (sg-SON) treated samples. In this part, cells were all transfected with GCN4-dCas13b. scFv-GGS6-FTO (WT), scFv-GGS⁶-FTO^{H231A D233A} (Mut), sgRNA (sg-SON) or pc0043 vector (sg-Control) were transfected as indicated for overall 48 hours.

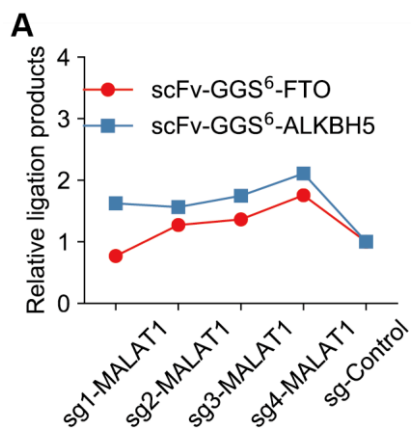


Figure S10 | Screen of sgRNA for MALAT1. (A) Measurement of m⁶A level on MALAT1 A2577 in individual groups. Relative ligation products of each group were quantified by qPCR. Cells were all transfected with GCN4-dCas13b. ScFv-GGS⁶-ALKBH5, scFv-GGS⁶-FTO and sgRNA were transfected as indicated for overall 48 hours.

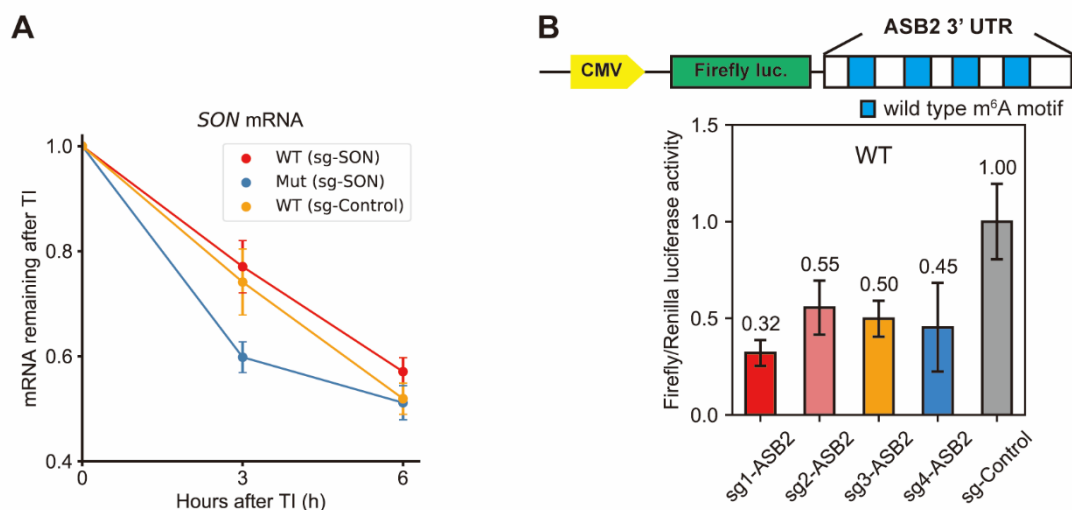


Figure S11 | Regulation of target RNA stability and expression in an m⁶A-dependent manner using TRADES system. (A) The mRNA lifetime of SON in HeLa cells. Cells were all transfected with GCN4-dCas13b. scFv-GGS⁶-FTO (WT), scFv-GGS⁶-FTO^{H231A D233A} (Mut), sgRNA (sg-SON) or pc0043 vector (sg-Control) were transfected as indicated for overall 48 hours. And actinomycin D was added to 5 μ g/mL at 6 hours, 3 hours and 0 hour before cell scraping collection. The total RNA was isolated and then the SON abundance was analyzed by RT-qPCR. The mRNA remaining quantitative values at time 0 h were arbitrarily adjusted to 1. Scatters represent mean \pm SD from two independent experiments (n = 2). (B) Schematic representation of constructs used in dual-luciferase analysis. ASB2 3'-UTR was cloned 3' downstream of the firefly luciferase. TRADES was applied to targeted demethylate ASB2 3'-UTR. The Firefly/Renilla luciferase activity was accessed by Dual-Luciferase Reporter Assay System. All groups were transfected with GCN4-dCas13b and scFv-GGS⁶-FTO, the sgRNA was transfected as indicated. Bars represent mean \pm SD from two independent experiments (n = 2).

Table S1: Primers used for subcloning.

Name	Sequence (5'→3')
XTEN-FTO-F1	5'-AGCGGCAGCGAGACTCCCGGGACCTCAGAGTCCGCC ACACCCGAAAGTATGAAGCGCACCCCGACTGC-3'
XTEN-FTO-BamHI F2	5'-GTGGTGGTTCAGGAGGCGGCGGATCCAGCGGCAGCG AGACTCCCGG-3'
XTEN-FTO-RsrII R	5'-AGGATAAGCTTGTACTCTTCGGTCCGGGGTTTTGCTT CCAGAAGCT-3'
GGG ⁶ -FTO-F1	5'-GGCGGTAGTGGAGGAAGCGGGGGGAGCGGAGGGAG TGGTGGATCCGGCGGCTCCATGAAGCGCACCCCGACTG C-3'
GGG ⁶ -FTO-BamHI F2	5'-GTGGTGGTTCAGGAGGCGGCGGATCCGGCGGTAGTG GAGGAAGCGG-3'
GGG ⁶ -FTO-RsrII R	The same as "XTEN FTO -RsrII R"
GGG ⁶ -ALKBH5-F1	5'-GGCGGTAGTGGAGGAAGCGGGGGGAGCGGAGGGAG TGGTGGATCCGGCGGCTCCATGGCGGCCGCCAGCGGCT AC-3'
GGG ⁶ -ALKBH5-Ba mHI-F2	5'-GTGGTGGTTCAGGAGGCGGCGGATCCGGCGGTAGTG GAGGAAGCGG-3'
GGG ⁶ -ALKBH5-Rsr II R	5'-CAGGATAAGCTTGTACTCTTCGGACCGGTGCCGCCG CATCTTCACCT-3'
ALKBH5 ^{H204A} -F	5'-CATCGTGTCTGCCGTGGACCCCATCCACATCTTCGAG CGCCCATCGT-3'
ALKBH5 ^{H204A} -R	5'-TGGGGTCCACGGCAGACACGATGCAGCCCGCGGGCT GGTAGTCGTTGA-3'
C-GCN4-KpnI-F	5'-AATTGGTACCCCAAGAAAAACGCAAGGT-3'
C-GCN4-XbaI-R	5'-AATTTCTAGATCAATGGTGATGGTGATGAT-3'
N-dCas13b-HindIII- F	5'-AAGCTTATGCCTAAGAAAAAGAGGAAGGTGGAATTC ATGAACATCCCGCTCTGGT-3'
N-dCas13b-EcoRV- R	5'-AATTGATATCCTCTTTGGACACGA-3'
GGG ⁶ -EcoRV-F	5'-ATCGGCGGTAGTGGAGGAAGCGGGGGGAGCGGAGG GAGTGGTGGATCCGGCGGCTCCGGTAC-3'

28S sgRNA4 B	5'-CACCCCGGGCGCGACCCGCTCCGGGGACAGTGCCAG GTGGGGAGTTTGACTGGGGCGGTACACCTGTCAAACGG TAACGCAGGTGTCCC-3'
MALAT1 sgRNA1 T	5'-CACCGTCAAAGTCCAATGCAAAAACATTAAGTTGG- 3'
MALAT1 sgRNA1 B	5'-CAACCCAACCTTAATGTTTTTGCATTGGACTTTGAC-3'
MALAT1 sgRNA2 T	5'-CACCGTCAAAGTCCAATGCAAAAACATTAAGTTGGT AATTACTCTTGATCTTGAA-3'
MALAT1 sgRNA2 B	5'-CAACTTCAAGATCAAGAGTAATTACCAACTTAATGT TTTTGCATTGGACTTTGAC-3'
MALAT1 sgRNA3 T	5'-CACCGTCAAAGTCCAATGCAAAAACATTAAGTTGGT AATTACTCTTGATCTTGAATTACTTCCGTTACGAAAGTC -3'
MALAT1 sgRNA3 B	5'-CAACGACTTTCGTAACGGAAGTAATTCAAGATCAAG AGTAATTACCAACTTAATGTTTTTGCATTGGACTTTGAC -3'
MALAT1 sgRNA4 T	5'-CACCGTCAAAGTCCAATGCAAAAACATTAAGTTGGT AATTACTCTTGATCTTGAATTACTTCCGTTACGAAAGTC CTTCACATTTTTCA-3'
MALAT1 sgRNA4 B	5'-CAACTGAAAAATGTGAAGGACTTTCGTAACGGAAGT AATTCAAGATCAAGAGTAATTACCAACTTAATGTTTTT GCATTGGACTTTGAC-3'
MALAT1 sgRNA-A T	5'-CACCGAATGCAAAAACATTAAGTTGGTAATTACTCT TGATCTTGAATTACTTCCGTTACGAAAGTCCTTCACATT TTTCAAACCTAAGCT-3'
MALAT1 sgRNA-A B	5'-CAACAGCTTAGTTTTGAAAAATGTGAAGGACTTTCGT AACGGAAGTAATTCAAGATCAAGAGTAATTACCAACTT AATGTTTTTGCATTC-3'
MALAT1 sgRNA-B T	5'-CACCGCATTAAAGTTGGTAATTACTCTTGATCTTGAAT TACTTCCGTTACGAAAGT-3'
MALAT1 sgRNA-B B	5'-CAACACTTTCGTAACGGAAGTAATTCAAGATCAAGA GTAATTACCAACTTAATGC-3'

MALAT1 sgRNA-C T	5'-CAACGAAGGCCTTAAATATAGTAGCTTAGTTTGAAA AATGTGAAGGACTTTCGTAACGGAAGTAATTCAAGATC AAGAGTAATTACCAC-3'
MALAT1 sgRNA-C B	5'-CACCGTCTTGATCTTGAATTACTTCCGTTACGAAAGT CCTTCACATTTTTCAAACCTAAGCTACTATATTTAAGGCC TTCCAAATTCTTC-3'
SON sgRNA1 T	5'-CACCGCTGGGAGTCCATGGTGTGGACGCTAGCAT- 3'
SON sgRNA1 B	5'-CAACATGCTAGCGTCCAACACCATGGACTCCCAGC- 3'
SON sgRNA2 T	5'-CACCGCTGGGAGTCCATGGTGTGGACGCTAGCATT TGGGAGTCCATGGTGTGG-3'
SON sgRNA2 B	5'-CAACCCAACACCATGGACTCCCAAATGCTAGCGTCC AACACCATGGACTCCCAGC-3'
SON sgRNA3 T	5'-CACCGCTGGGAGTCCATGGTGTGGACGCTAGCATT TGGGAGTCCATGGTGTGGATGCTAATATATGGGTCTC C-3'
SON sgRNA3 B	5'-CAACGGAGACCCATATATTAGCATCCAACACCATGG ACTCCCAAATGCTAGCGTCCAACACCATGGACTCCCAG C-3'
SON sgRNA4 T	5'-CACCGCTGGGAGTCCATGGTGTGGACGCTAGCATT TGGGAGTCCATGGTGTGGATGCTAATATATGGGTCTC CATGGTGTTAGAAGC-3'
SON sgRNA4 B	5'-CAACGCTTCTAACACCATGGAGACCCATATATTAGC ATCCAACACCATGGACTCCCAAATGCTAGCGTCCAACA CCATGGACTCCCAGC-3'
ASB2 sgRNA1 T	5'-CACCGGCTACTCCTCTCTCCCCGTGGCCCCAGTTACT GGGTGTTCTCGTATTTTCAGGTATCTAATCAGCCTGCCTG GGAGCGGCAAGGT-3'
ASB2 sgRNA1 B	5'-CAACACCTTGCCGCTCCCAGGCAGGCTGATTAGATA CCTGAAATACGAGAACACCCAGTAACTGGGGCCACGG GGAGAGAGGAGTAGCC-3'

ASB2 sgRNA2 T	5'-CACCGGAGAGGGAGGCAGCCTGCAGCCTCGTCTGTC ACCAGGTCCCCTTGGAGTTGGGAACACCGACGTCCTGA G-3'
ASB2 sgRNA2 B	5'-CAACCTCAGGACGTCCGGTGTCCCAACTCCAAGGGG ACCTGGTGACAGACGAGGCTGCAGGCTGCCTCCCTCTC C-3'
ASB2 sgRNA3 T	5'-CACCGCAAATGATTCTTCTCCTTGACACATTCTGTTC TCTGCTCTGGCCAAAGCTCTGGGCCCTGAGACCCAGTG- 3'
ASB2 sgRNA3 B	5'-CAACCACTGGGTCTCAGGGCCAGAGCTTTGGCCAG AGCAGAGAACAGAATGTGTCAAGGAGAAGAATCATT GC-3'
ASB2 sgRNA4 T	5'-CACCGGAGAAAGCTCTGAAGTCAAGTGGTGAGTTTT CCAGAACAAGTGGAGGGGCACAGGGAAGGCTCTGAGC ACCACCTTCCCCAGAA-3'
ASB2 sgRNA4 B	5'-CAACTTCTGGGGAAGGTGGTGCTCAGAGCCTTCCT GTGCCCTCCACTTGTCTGGAAAACCTCACCCTTGACT TCAGAGCTTTCTCC-3'
HBV sgRNA1 T	5'-CACCGGTCAATGTCCATGCCCCAAAGCCACCCAAG- 3'
HBV sgRNA1 B	5'-CAACCTTGGGTGGCTTTGGGGCATGGACATTGACC-3'
HBV sgRNA2 T	5'-CACCGGTCAATGTCCATGCCCCAAAGCCACCCAAGG CACAGCTTGGAGGCTTGAA-3'
HBV sgRNA2 B	5'-CAACTTCAAGCCTCCAAGCTGTGCCTTGGGTGGCTTT GGGGCATGGACATTGACC-3'
HBV sgRNA3 T	5'-CACCGGTCAATGTCCATGCCCCAAAGCCACCCAAGG CACAGCTTGGAGGCTTGAACAGTGGGACATGTACAAG AG-3'
HBV sgRNA3 B	5'-CAACCTCTTGACATGTCCCACTGTTCAAGCCTCCAA GCTGTGCCTTGGGTGGCTTTGGGGCATGGACATTGACC- 3'

HBV sgRNA4 T	5'-CACCGGTCAATGTCCATGCCCAAAGCCACCCAAGG CACAGCTTGGAGGCTTGAACAGTGGGACATGTACAAG AGATGATTAGGCAGAG-3'
HBV sgRNA4 B	5'-CAACCTCTGCCTAATCATCTCTTGTACATGTCCCCT GTTCAAGCCTCCAAGCTGTGCCTTGGGTGGCTTTGGGG CATGGACATTGACC-3'
HIV sgRNA1 T	5'-CACCGATTGAGGCTGCGCCCATAGTGCTTCCTGCT-3'
HIV sgRNA1 B	5'-CAACAGCAGGAAGCACTATGGGCGCAGCCTCAATC- 3'
HIV sgRNA2 T	5'-CACCGATTGAGGCTGCGCCCATAGTGCTTCCTGCTGC TCCCAAGAACCCAAGGAA-3'
HIV sgRNA2 B	5'-CAACTTCCTTGGGTTCTTGGGAGCAGCAGGAAGCAC TATGGGCGCAGCCTCAATC-3'
HIV sgRNA3 T	5'-CACCGATTGAGGCTGCGCCCATAGTGCTTCCTGCTGC TCCCAAGAACCCAAGGAACAAAGCTCCTATTCCCCTG -3'
HIV sgRNA3 B	5'-CAACCAGTGGGAATAGGAGCTTTGTTTCCTTGGGTTCT TGGGAGCAGCAGGAAGCACTATGGGCGCAGCCTCAAT C-3'
HIV sgRNA4 T	5'-CACCGATTGAGGCTGCGCCCATAGTGCTTCCTGCTGC TCCCAAGAACCCAAGGAACAAAGCTCCTATTCCCCTG CTCTTTTTTCTCTC-3'
HIV sgRNA4 B	5'-CAACGAGAGAAAAAGAGCAGTGGGAATAGGAGCT TTGTTTCCTTGGGTTCTTGGGAGCAGCAGGAAGCACTAT GGGCGCAGCCTCAATC-3'

Table S2: Primers used for RT-qPCR.

Name	Sequence (5'->3')
qPCR-F for SELECT	5'-ATGCAGCGACTCAGCCTCTG-3'
qPCR-R for SELECT	5'-TAGCCAGTACCGTAGTGCGTG-3'
MALAT1 qPCR-F	5'-GACGGAGGTTGAGATGAAGCT-3'
MALAT1 qPCR-R	5'-ATTCGGGGCTCTGTAGTCCT-3'
SON qPCR-F	5'-GAGCCCCCAGTAGCAAAAAGT-3'
SON qPCR-R	5'-CCGATGGTACGTCTACAGGC-3'
HPRT1 qPCR-F	5'-TGACACTGGCAAAACAATGCA-3'
HPRT1 qPCR-R	5'-GGTCCTTTTCACCAGCAAGCT-3'
GAPDH qPCR-F	5'-TGCACCACCAACTGCTTAGC-3'
GAPDH qPCR-R	5'-GGCATGGACTGTGGTCATGAG-3'
HBV qPCR-F	5'-GTCAACGACCGACCTTG-3'
HBV qPCR-R	5'-TGATTAGGCAGAGGTGAAAAAG-3'
ASB2 qPCR-F	5'-CGTGGTGCAGTTCTGTGAGT-3'
ASB2 qPCR-R	5'-GTGAGCCAGAGGTCTTGGAG-3'
HIV qPCR-F	5'-GGGCTAATTCACCTCCCAACGA-3'
HIV qPCR-R	5'-ATCTGATCCCTGGCCCTGGT-3'

Table S3: Primers used in SELECT.

Name	Sequence (5'→3')
MALAT1 m ⁶ A Up	5'-TAGCCAGTACCGTAGTGCGTGggatttaaaaaataatcttaactcaaag-3'
MALAT1 m ⁶ A Down	5'-pos/ccaatgcaaaaacattaagtCAGAGGCTGAGTCGCTGCAT-3'
SON A2699 Up	5'-TAGCCAGTACCGTAGTGCGTGtggatgctagcatctgggag-3'
SON A2699 Down	5'-pos/ccatggtgttgacgctagcCAGAGGCTGAGTCGCTGCAT-3'
SON A2759 Up	5'-TAGCCAGTACCGTAGTGCGTGtagttgctaacaatctgggag-3'
SON A2759 Down	5'-pos/ccatggtgctagacgctaacCAGAGGCTGAGTCGCTGCAT-3'
SON A2789 Up	5'-TAGCCAGTACCGTAGTGCGTGtagttgctaacaatctgggag-3'
SON A2789 Down	5'-pos/ccatggagctagttgctaacCAGAGGCTGAGTCGCTGCAT-3'
SON A2819 Up	The same as "SON m ⁶ A2789 Up"
SON A2819 Down	The same as "SON m ⁶ A2789 Down"
HBV m ⁶ A Up	5'-TAGCCAGTACCGTAGTGCGTGcaaattctttataagggtcaatg-3'
HBV m ⁶ A Down	5'-pos/ccatgccccaaagccaccaCAGAGGCTGAGTCGCTGCAT-3'
ASB2-1 m ⁶ A Up	5'-TAGCCAGTACCGTAGTGCGTGgtcctgagacttagtaagaagag-3'
ASB2-1 m ⁶ A Down	5'-phos/ctgaggggctactcctctctCAGAGGCTGAGTCGCTGCAT-3'
HIV m ⁶ A Up	5'-TAGCCAGTACCGTAGTGCGTGtaattgtctggcctgtaccg-3'
HIV m ⁶ A Down	5'-phos/cagcgtcattgaggctgcgc-cagaggctgagtcgctgcat-3'
MALAT1 2515 m ⁶ A Up	5'-TAGCCAGTACCGTAGTGCGTGAattactccgttacgaaag-3'
MALAT1 2515 m ⁶ A Down	5'-phos/ccttcacattttcaaactaagCAGAGGCTGAGTCGCTGCAT-3'
MALAT1 2611 m ⁶ A Up	5'-TAGCCAGTACCGTAGTGCGTGcagctgtcaattaatgctag-3'
MALAT1 2611 m ⁶ A Down	5'-phos/cctcaggatttaaaaaataatcttaacCAGAGGCTGAGTCGCTGCAT-3'

Table S4: The exact sequences of the reporters used in dual-luciferase assay.

Wild type and mutant ASB2-3'-UTR were inserted into downstream of firefly luciferase of pMIR-REPORT vector (Luciferase miRNA Expression Reporter Vector, Ambion);

(1) ASB2-3'-UTR with wild-type m⁶A sites:

ATGACTAGACTAGTGGCCACGGGGAGAGAGGAGTAGCCCCTCAGACTCTTCTTA
 CTAAGTCTCAGGACGTCGGTGTTCCCAACTCCAAGGGGACCTGGTGACAGACGAG
 GCTGCAGGCTGCCTCCCTCTCAGCCTGGACAGCTACCAGGATCTCACTGGGTCTC
 AGGGCCCAGAGCTTTGGCCAGAGCAGAGAACAGAATGTGTCAAGGAGAAGAATC
 ATTTGTTTACAAACTGATGAGCAGATCCCAGACCTTCTCTACCTTCAGGAATGGC
 AGAAACCTCTATTCCTGGGGCCAGGGCAGAGCTTGAGGTGTTCTGGGGAAGGTG
 GTGCTCAGAGCCTTCCCTGTGCCCTCCACTTGTTCTGGAAACTCACCACTTGAC
 TTCAGAGCTTTCTCTCCAAAGACTAAGATGAAGACGTGGCCCAAGGTAGGGGGT
 AGGGGGAGCCTGGAAGCTTGGGATCTA

ASB2-3'-UTR with mutant m⁶A sites:

ATGACTAGACTAGTGGCCACGGGGAGAGAGGAGTAGCCCCTCAGTCTCTTCTTA
 CTAAGTCTCAGGACGTCGGTGTTCCCAACTCCAAGGGGACCTGGTGACAGACGAG
 GCTGCAGGCTGCCTCCCTCTCAGCCTGGTCAGCTACCAGGATCTCACTGGGTCTC
 AGGGCCCAGAGCTTTGGCCAGAGCAGAGAACAGAATGTGTCAAGGAGAAGAATC
 ATTTGTTTACAATCTGATGAGCAGATCCCAGACCTTCTCTACCTTCAGGAATGGC
 AGAAACCTCTATTCCTGGGGCCAGGGCAGAGCTTGAGGTGTTCTGGGGAAGGTG
 GTGCTCAGAGCCTTCCCTGTGCCCTCCACTTGTTCTGGAAACTCACCACTTGAC
 TTCAGAGCTTTCTCTCCAAAGTCTAAGATGAAGACGTGGCCCAAGGTAGGGGGT
 AGGGGGAGCCTGGAAGCTTGGGATCTA