

Section A: Materials and Methods

A1. Materials and Instruments

A1.1. Oligonucleotides and Materials.

The DNA oligonucleotides (Table S1) were obtained from Shanghai Sangon Biological Engineering Technology & Services Co., Ltd (Shanghai, China), and purified by 10% denaturing (8 M urea) polyacrylamide gel electrophoresis (dPAGE) or high-performance liquid chromatograph (HPLC). Taq DNA polymerase (Taq DP), T4 DNA ligase (T4 DL), and deoxyribonucleoside 5'-triphosphates (dNTPs) were purchased from Sangon Biotech. Adenosine triphosphate (ATP), Uracil-DNA glycosylase (UDG), alkaline phosphatase (ALP), glutathione (GSH), glucose, and thrombin were purchased from Shanghai Sangon Biological Engineering Technology & Services Co., Ltd (Shanghai, China). Bovine Serum Albumin (BSA), α -KG, and L-ascorbic were purchased from Dakewe Biotech Co., Ltd. (Beijing, China). *EcoR* V was purchased from Takara (Beijing, China). T4 polynucleotide kinase (PNK) was obtained from Thermo Fisher Scientific. Recombinant human ALKBH3 protein (81130) was purchased from Active Motif (Carlsbad, USA). SYBR™ Gold Nucleic Acid Gel Stain (10,000 × Concentrate in DMSO) was purchased from Thermo Fisher Scientific. HUHS015, Entacapone, and Thiram were purchased from MedChemExpress (China). Dulbecco's modified Eagle's medium (DMEM), Fetal Bovine Serum (FBS), Trypsin-EDTA (0.25%, phenol red), Opti-MEM, and Lipofectamine-3000 were purchased from Thermo Fisher Scientific (Waltham, USA). 4',6-Diamidino-2-phenylindole (DAPI), and 4% paraformaldehyde were purchased from Beijing Solarbio Science & Technology Co., Ltd. (Beijing, China). PC-3 cells (human prostate cancer cells) and WPMY-1 cells (human normal prostate matrix immortalized cells) were gained from cell-bioscience with STR analysis (Shanghai, China). All other chemicals were purchased from Sigma-Aldrich and used without further purification.

A1.2. Instruments.

The fluorescent images of gels were obtained using a Typhoon 5 variable mode imager (GE Healthcare, US) and analyzed using Image Quant software (Molecular Dynamics). Fluorescence measurements were performed with a Cary Eclipse fluorescence spectrophotometer (Agilent, US). Confocal imaging experiments were carried out by a laser scanning confocal microscope (FV1000, Olympus, Japan). Flow cytometry results were obtained using a FACScan cytometer (FACSCanto, BD, US).

A1.3. Buffers used in this work.

(1) 1 × PNK buffer: 50 mM Tris-HCl, 10 mM MgCl₂, 5 mM DTT, and 0.1 mM spermidine, pH 7.6.

(2) 1 × T4 DNA ligase buffer: 40 mM Tris-HCl, 10 mM MgCl₂, 10 mM DTT, 0.5 mM ATP, pH 7.8.

(3) 1 × *EcoRV* buffer: 50 mM Tris-HCl (pH 7.5), 10 mM MgCl₂, 1 mM Dithiothreitol, 100 mM NaCl.

(4) 1 × *EcoRV* loading buffer: 0.09% SDS, 5% Glycerol, 0.005% Bromophenol Blue.

(5) 1 × selection buffer (1 × SB): 50 mM HEPES, 150 mM NaCl, 50 mM KCl, 15 mM MgCl₂, 5 mM MnCl₂, and 0.01% Tween 20, pH 7.5.

(6) 1 × PCR buffer: 75 mM Tris-HCl, pH 9.0, 2 mM MgCl₂, 50 mM KCl, 20 mM (NH₄)₂SO₄.

(7) 2 × urea PAGE loading buffer: 80 mM EDTA (pH 8.0), 16 M urea, 180 mM Tris, 180 mM boric acid, 20% sucrose (w/v), 0.05% xylene cyanol, and 0.05% bromophenol blue.

(8) 1 × ALKBH3 reaction buffer: 50 mM HEPES, 50 μM (NH₄)₂Fe(SO₄)₂·6H₂O, 1 mM α-KG, 2 mM L-ascorbic acid and 50 μg/mL BSA, pH 7.0.

A2. Methods

A2.1. In vitro selection procedures.

Ligation of DL1 to S1^A and purification (step I). DL1 (500 pmol) was phosphorylated at 37 °C with 10 U of PNK in 50 μL of 1 × PNK buffer containing 2 mM ATP for 40 min. Then, 10 μL of 10 × T4 DNA ligase buffer, S1^A (600 pmol), and DS1 (600 pmol) were added and the volume was adjusted to 96 μL with ddH₂O. The mixture was heated to 90 °C for 2 min, and then cooled at RT for 15 min. 4 μL of T4 DL (5 U/μL) was added to the mixture and incubated at room temperature (RT) for 2.5 h. The obtained DL1-S1^A cis constructs were concentrated by standard ethanol precipitation and purified by 10% dPAGE.

Counter selection (step II). The purified DL1-S1^A was dissolved in 20 μL of ddH₂O and quantified by NanoDrop. 50 μL of 2 × SB was added and adjusted the volume to 100 μL using ddH₂O. The mixture was heated at 90 °C for 2 min and cooled to RT for 15 min. Followed by incubation at RT for 24 h, the reaction was stopped by ethanol precipitation.

Generation of DL1 (step III). The uncleaved DL1-S1^A molecules were purified by 10% dPAGE, dissolved in 20 μL of ddH₂O. This was followed by the addition of DS1 (60 pmol), 10 × *EcoRV* buffer (10 μL) and *EcoRV* (4 μL, 15 U/μL) in a total volume of 100 μL. Followed by incubation at 37 °C for 3 h, the reaction was stopped by ethanol precipitation. The DL1 molecules from

step III were purified by 10% dPAGE, dissolved in 20 μ L of ddH₂O and stored at -20 °C.

Ligation of DL1 to S2^{m1A} (step IV). The obtained DL1 was phosphorylated at 37 °C with 10 U of PNK in 50 μ L of 1 \times PNK buffer containing 2 mM ATP for 40 min. Then, 10 μ L of 10 \times T4 DL buffer, S2^{m1A} (600 pmol), and DS1 (600 pmol) were added and the volume was adjusted to 96 μ L with ddH₂O. The mixture was heated to 90 °C for 2 min, and then cooled at RT for 15 min. 4 μ L of T4 DL (5 U/ μ L) was added to the mixture and incubated RT for 2.5 h. The obtained DL1-S2^{m1A} cis constructs were concentrated by standard ethanol precipitation and purified by 10% dPAGE.

Positive selection (step V). The purified DL1-S2^{m1A} molecules (100 pmol) was mixed with 50 μ L of 2 \times SB and adjusted the volume to 100 μ L using ddH₂O. The mixture was heated at 90 °C for 2 min, and cooled to RT for 15 min. Followed by incubation at RT for 12 h, the reaction was stopped by ethanol precipitation. The cleaved molecules from step V were purified by 10% dPAGE, dissolved in 20 μ L of ddH₂O and stored at -20 °C until use.

PCR (step VI). PCR1: 50 μ L of PCR mixture containing the purified cleaved products, 1 μ M each of FP and RP1, 60 μ M each of dNTPs (dATP, dCTP, dGTP, and dTTP), 1 \times PCR buffer and 5 U of Taq DP, was subjected to the following steps: 95 °C for 1 min; 11-15 cycles of 94 °C for 1 min, 52 °C for 45 s and 72 °C for 30 s; 72 °C for 5 min using a Bio-Rad thermal cycler. PCR2: 5 μ L of the PCR1 product was diluted with ddH₂O to 50 μ L, 1-5 μ L of which was used as the template for PCR2 using FP and RP2 according to the same protocol for PCR1. The numbers of cycles between different rounds were adjusted, typically between 12 and 14 cycles, to achieve full amplification. The PCR2 products were concentrated by ethanol precipitation and purified by 10% dPAGE.

After 16 rounds of selection, the enriched libraries from round 16 were subjected to deep sequencing using the MiSeq (Illumina) sequencing platform.

A2.2. Kinetic analysis (Figures 2a).

2 μ L of 5 μ M RCD1-S1^A (or S2^{m1A}), 50 μ L of 2 \times SB and 48 μ L ddH₂O were incubated at RT for 1 min, 5 min, 10 min, 20 min, 30 min, 60 min, 120 min, and 180 min before ethanol precipitation. The resultant products were analyzed by 10% dPAGE (8 M urea). Cleavage yields were determined by measuring the fluorescent intensity of the corresponding bands. Apparent rate constants were determined by curve-fitting cleavage yield versus time using Origin 8.0 where $Y = Y_{\max} [1 - e^{-kt}]$, Y_{\max} represents the maximal cleavage yield and k is the observed first-order rate constant (k_{obs}).

A2.3. Fluorescence analysis of trans-acting DNAzyme (Figures 3f).

Time-dependent fluorescence response of RCD1T/S^{m1A} was performed as follows: 10 μ L of 10 μ M RCD1T, 4 μ L of 5 μ M S^A/S^{m1A}, 36 μ L ddH₂O and 50 μ L of 2 \times SB were mixed in 96-well plates. Time-dependent fluorescence at $\lambda_{\text{ex}}/\lambda_{\text{em}} = 485 \text{ nm}/520 \text{ nm}$ was recorded every minute for 3 h.

A2.4. Evaluation of ALKBH3 inhibitors (Figure 4c).

500 nM ALKBH3 was pre-incubated with different concentrations of inhibitor (HUHS015, Entacapone, and Thiram) in 1 \times ALKBH3 reaction buffer for 20 min. 2 μ M S^{m1A} was then added and incubated at 37 $^{\circ}$ C for 2 h. This was followed by the addition of 1 μ M RCD1T and 50 μ L of 2 \times SB (final volume: 100 μ L). The fluorescence signals were recorded for 30 min in a 96-well black microplate at $\lambda_{\text{ex}}/\lambda_{\text{em}} = 485 \text{ nm}/520 \text{ nm}$.

A2.5. Cell culture.

WPMY-1 cells (human normal prostate matrix immortalized cells) were cultivated in Dulbecco's Modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum (FBS) and antibiotics (100 U/mL penicillin and 100 U/mL streptomycin), PC-3 cells (human prostate cancer cells) were maintained in F12K medium supplemented with 10% fetal bovine serum, 100 U/mL penicillin and streptomycin. All cell lines were cultured in a humidified incubator at 37 $^{\circ}$ C with 5% CO₂. Cells were grown to approximately 80% confluence before harvesting, media was removed, and cells were washed twice with 1 mL of PBS. Cells were incubated with 1 mL of 0.25% trypsin-EDTA for 40 s to dissociate cells. The dissociated cells were collected by centrifugation at 900 rpm for 5 min. The supernatant was removed, and cells were resuspended in 1 mL of the complete growth medium and transferred to 35 mm glass-based dishes (for cell imaging) or 12-well plates (for flow cytometry assay).

A2.6. Microscopy confocal imaging assay (Figures 5b and 6a).

PC-3 cells were plated on a 35 mm glass-bottom dish (1 \times 10⁵ cells/dish) and incubated at 37 $^{\circ}$ C for 24 h. Cells were pretreated with HUHS015 (10 μ M) at 37 $^{\circ}$ C for 12 h, and then washed with 1 mL of 1 \times PBS three times (with each wash for 5 s). RCD1T (200 nM) and S^{m1A} (40 nM) (or other controls) were mixed in Opti-MEM (150 μ L), and were then mixed with Lipofectamine 3000 (3.5 μ L) dispersed in Opti-MEM (150 μ L) for 20 min at RT. This was followed by adding the above mixture to cells and incubated at 37 $^{\circ}$ C for 5 h. After washing three times with 1 \times PBS to remove the un-transfected RCD1T/S^{m1A}, cells were fixed in 800 μ L of 4% (w/v) paraformaldehyde for 10 min at RT. Subsequently, 1 mL 1 \times SB was added into the dishes and incubated for 30 min. The cells were then washed with 1 \times PBS three times, followed by incubating with WGA-Alexa 555 (5 μ g/mL) for 30 min to label the cell membrane, and DAPI (10 μ g/mL) for 10 min to label the nuclei,

respectively. The fluorescence images of cells were collected using laser scanning confocal microscope at 60 x magnification. The FAM, DAPI and WGA were measured under the excitation of 488 nm, 405 nm and 559 nm, and the quantitative data were calculated by ImageJ software.

For ALKBH3 inhibitors assay, PC-3 cells were treated with varying concentrations of HUHS015 (0, 0.01, 0.1, 1, and 10 μ M) for 12 h, followed by the transfection of RCD1T/S^{m1A} as described above.

For monitoring the response of RCD1T in different cells. WPMY-1 cells and PC-3 cells were seeded on a 35 mm glass-bottom dishes (1 x 10⁵ cells/dish) and incubated at 37 °C for 24 h without HUHS015. Following the protocols as described above, the cells were imaged.

A2.7. Flow cytometry assay (Figures 6b).

For flow cytometry analysis, WPMY-1 cells and PC-3 cells were seeded into 12-well plates and grown for 24 h to reach 70-80% confluency. After transfected with the RCD1T/S^{m1A} (or RCD1T/S^A) for 5 h, cells were washed three times with 1 x PBS. Then the protocol was similar to the one described in **A.2.6**. The obtained cells were detached from the 12-well plate by 0.05% trypsin. The suspended cells were centrifuged for 5 min at 900 rpm. After resuspended in 500 μ L of PBS, the cells were used for flow cytometry analysis (FACSCanto, BD, US). Fluorescence was determined by counting 10,000 usable events at a rate of 35 μ L/min, and the data were analyzed by FlowJo software.

The mean fluorescence intensity (MFI) was calculated directly from the software FlowJo and used the equation:

$$MFI = \sum \frac{F_x * C_x}{N_{total}}$$

where F_x is the fluorescence intensity value from the x-axis and C_x is the corresponding cell counts from the y-axis, and N_{total} is the total cell numbers counted for each sample.

For gating strategy, the live cell gate is set based on forward scatter (FSC) and side scatter (SSC) to exclude dead cells, cell debris and small particulate matter. The cells of interest that are being selected (gated) express FITC. Dead cells and cell debris that are not of interest and will be “gated out”. All subsequent analyses are conducted within this same live cell gate.

Section B: Supporting Tables and Figures.

B1. Supplementary Tables

Table S1. Sequences of DNA oligonucleotides used in this work.

Description	Sequence (5' - 3')
DNA library (DL1, 76 nt)	ATCAGACCAC AACGGTTTCC C-N ₄₀ -TAGCATAACC CCTTG
Unmodified A substrate (S1 ^A , 33 nt)	CTATGAACTG ACTrATGACCT CACTACCAAG GAT
Modified m ¹ A substrate (S2 ^{m1A} , 33 nt)	CTATGAACTG ACTm ¹ ATGACCT CACTACCAAG GAT
Truncated A substrate (S3 ^A , 26 nt)	CTG ACTrATGACCT CACFACCAAG GAT (F = fluorescein-dT)
Truncated m ¹ A substrate (S3 ^{m1A} , 26 nt)	CTG ACTm ¹ ATGACCT CACFACCAAG GAT (F = fluorescein-dT)
trans-acting A substrate (S ^A , 17 nt)	FTGACTrATGA CCTCACQ (F = fluorescein-dC; Q = BHQ1-dT)
trans-acting m ¹ A substrate (S ^{m1A} , 17 nt)	FTGACTm ¹ ATGA CCTCACQ (F = fluorescein-dC; Q = BHQ1-dT)
Forward primer (FP, 21 nt)	ATCAGACCAC AACGGTTTCC C
Reverse primer 1 (RP1, 15 nt)	CAAGGGGTTA TGCTA
Reverse primer 2 (RP2, 36 nt)	A ₂₁ /Spacer C9/CAAGGGGTTA TGCTA
DNA Splint (DS1, 24 nt)	TTGTGGTCTG ATATCCTTGG TAGT
RCD1 (75 nt)	ATCAGACCAC AACGGTTTCC CGGGTGCGGG GTGTTGCAT AAA ACTGTCA TTCAATGTCA TAGCATAACC CCTTG
RCD2 (76 nt)	ATCAGACCAC AACGGTTTCC CCAGTTGAGG TTGCATTAAT CTGTCATTGT CTACGTTGTT ATAGCATAAC CCCTTG
RCD3 (76 nt)	ATCAGACCAC AACGGTT TCC CAGAGGTGAC CACAGATGTC GTGCAACATA TTGAGCCCGT GTAGCATAAC CCCTTG
RCD4 (76 nt)	ATCAGACCAC AACGGTTTCC CGAGGTGGTT GCATAAACCT GTCACGTTCT CCTGGGCGCT ATAGCATAAC CCCTTG
RCD5 (75 nt)	ATCAGACCAC AACGGTTTCC CTGGCTACCG GTGCGATGTG TTGCATTAAT CTGTCAGTCC TAGCATAACC CCTTG
RCD1S (54 nt)	ATCAGACCAC AACGGTTT GT GGTTCATAA AACTGTCATT CAATGTCATA GCAT
RCD1T (63 nt)	AGTGAGGATA TCAGACCACA ACGGTTT GTG GTTCATAAA ACTGTCATTC AATGTCATAG CAT
Mutant RCD1T (RCD1TM, 63 nt)	AGTGAGGATA TCAGACCACA ACGGTTT GTG GTTCGATTA ACTGTCATTC AATGTCATAG CAT

B2. Supplementary Figures

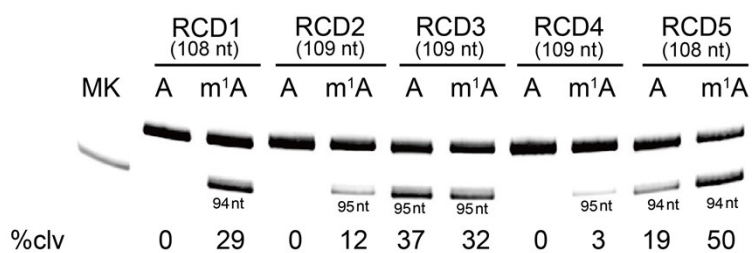


Fig. S1. 10% dPAGE analysis of the cleavage activity of top 5 RCDs towards S1^A and S2^{m¹A}, respectively. Reaction time: 60 min; Reaction temperature: 25 °C. MK, marker (94 nt); %clv, %cleavage.

Experimental details: The cleavage reactions were carried out in 1× SB. The protocol was similar to the one described in **A.2.2.** except that: RCD1, RCD2, RCD3, RCD4 and RCD5 were tested.

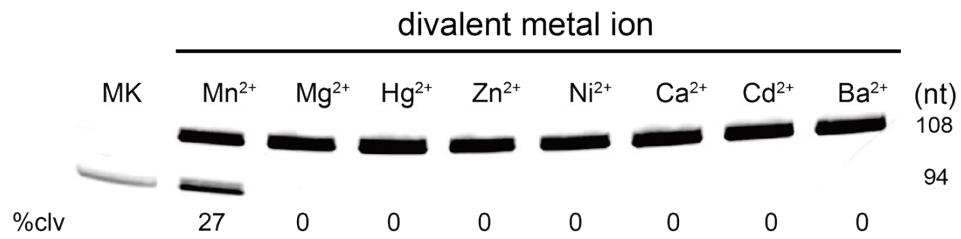


Fig. S2. 10% dPAGE analysis of the cleavage activity of RCD1-S2^{m1A} in the presence of various divalent metal ions. Reaction time: 60 min; Reaction temperature: 25 °C. MK, marker (94 nt); %clv, %cleavage.

Experimental details: The protocol was similar to the one described in **A2.2.** except that: Hg²⁺, Zn²⁺, Ni²⁺, Cd²⁺, Ca²⁺, Cd²⁺ and Ba²⁺ with a final concentration of 5 mM was used in 1 × SB.

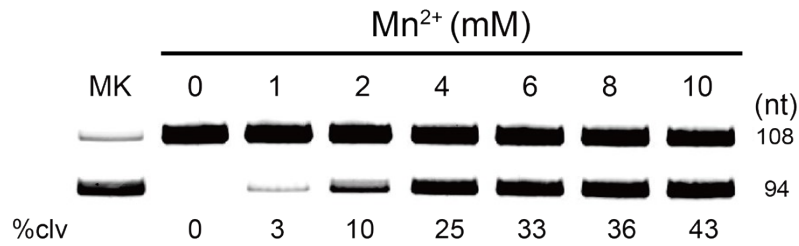


Figure S3. 10% dPAGE analysis of the cleavage activity of RCD1-S2^{m1A} at different Mn²⁺ concentrations. Reaction time: 60 min; Reaction temperature: 25 °C. MK, markers (108 nt and 94 nt); %clv, %cleavage.

Experimental details: The protocol was similar to the one described in **A2.2.** except that: different concentrations of MnCl₂ ranging from 1 mM to 10 mM (final concentration) were included in 1 × SB.

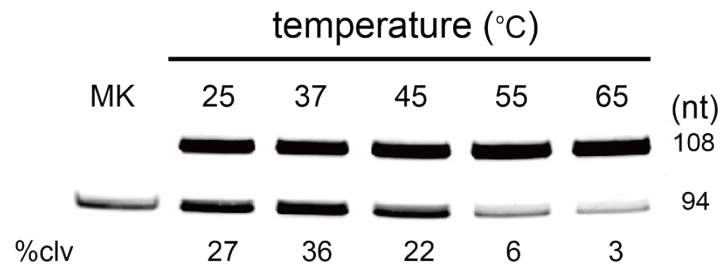


Figure S4. 10% dPAGE analysis of the cleavage activity of RCD1-S2^{m1A} at various reaction temperatures. Reaction time: 60 min. MK, marker (94 nt); %clv, %cleavage.

Experimental details: The protocol was similar to the one described in **A2.2.** except that: different reaction temperatures ranging from 25 °C to 65 °C were used.

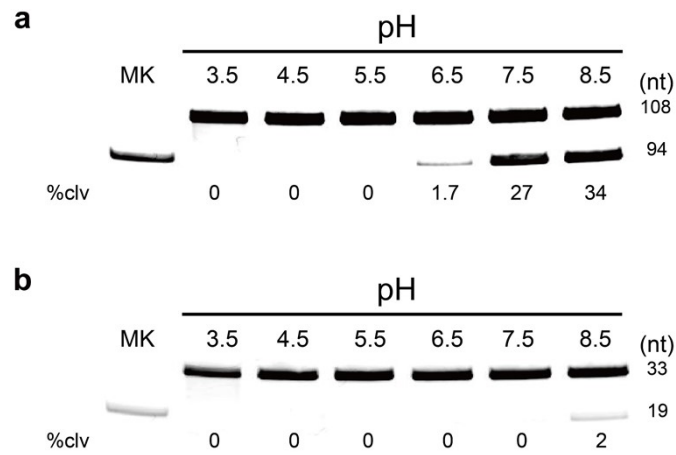


Fig. S5. 10% dPAGE analysis of the cleavage activity of a) RCD1-S2^{m1A} and b) S2^{m1A} at different pHs. Reaction time: 60 min; Reaction temperature: 25 °C. MK, marker (94 nt or 19 nt); %clv, %cleavage.

Experimental details: The protocol was similar to the one described in **A2.2.** except that: The solution pH was adjusted with the following buffering reagents (each used at 50 mM in 1 × SB): acetate for pH 3.5-5.5, MES for pH 6.5, and HEPES for pH 7.5-8.5 at 25 °C.

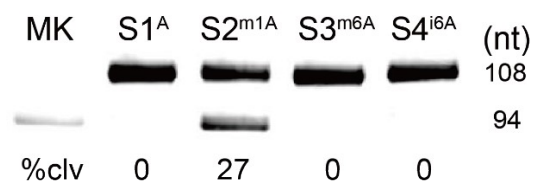


Fig. S6. 10% dPAGE analysis of the selectivity of RCD1 towards S1^A, S2^{m1A}, S3^{m6A} and S4^{i6A}, respectively. Reaction time: 60 min; Reaction temperature: 25 °C. MK, marker (94 nt); %clv, %cleavage.

Experimental details: The protocol was similar to the one described in **A.2.2.** except that: substrates S3^{m6A} and S4^{i6A} were used.

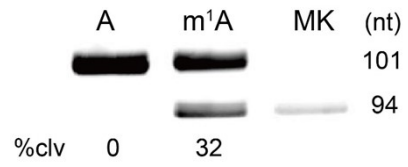


Fig. S7. 10% dPAGE analysis of the activity of RCD1S towards S3^A and S3^{m¹A}. Reaction time: 60 min; Reaction temperature: 25 °C. MK, marker (94 nt); %clv, %cleavage.

Experimental details: The protocol was similar to the one described in **A.2.2**.

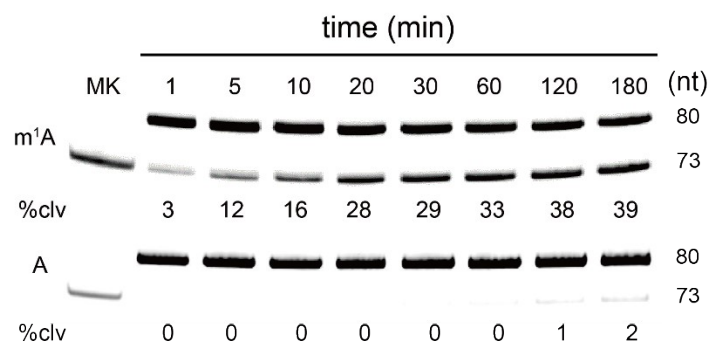


Fig. S8. 10% dPAGE analysis of the kinetic responses of RCD1S towards S3^A and S3^{m1A}, respectively. Reaction temperature: 25 °C. MK, marker (73 nt); %clv, %cleavage.

Experimental details: The protocol was similar to the one described in **A.2.2.** except that: RCD1S-S3^A (or S3^{m1A}) was used.

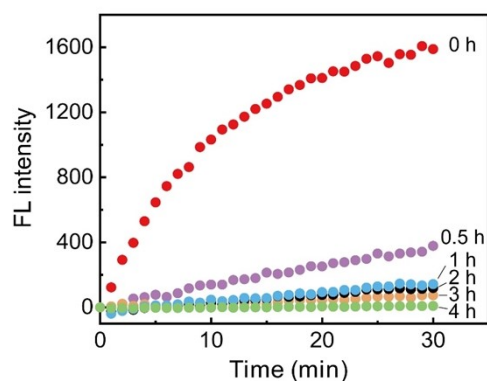


Fig. S9. Real-time fluorescence responses of RCD1T/S^{m1A} following incubation with ALKBH3 for a different period of time (0, 0.5, 1, 2, 3, 4 h).

Experimental details: 2 μM S^{m1A} and 500 nM ALKBH3 were pre-incubated in 1 \times ALKBH3 reaction buffer for a different period of time (0, 0.5, 1, 2, 3, 4 h) at 37 $^{\circ}\text{C}$. This was followed by the addition of 1 μM RCD1T and 50 μL of 2 \times SB (final volume: 100 μL). The fluorescence signals were recorded for 30 min in a 96-well black microplate at $\lambda_{\text{ex}}/\lambda_{\text{em}} = 485 \text{ nm}/520 \text{ nm}$.

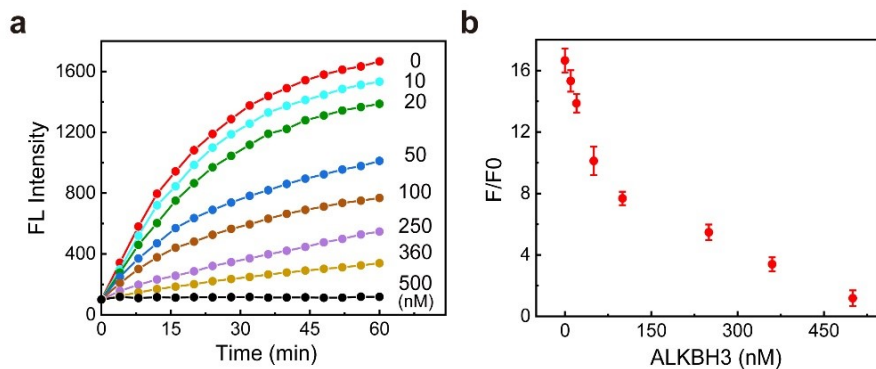


Fig. S10. a) Real-time fluorescence responses of RCD1T/S^{m1A} in response to different ALKBH3 concentrations (0, 10, 20, 50, 100, 250, 360, and 500 nM). b) Fluorescence responses as a function of ALKBH3 concentrations. The data obtained at 60 min were normalized using the following equation: F/F_0 , where F is the fluorescence intensity of each sample, F_0 is the initial reading in the absence of ALKBH3.

Experimental details: 2 μM S^{m1A} and ALKBH3 with different concentrations was pre-incubated in 1 \times ALKBH3 reaction buffer for 2 h at 37 $^{\circ}\text{C}$. This was followed by the addition of 1 μM RCD1T and 50 μL of 2 \times SB (final volume: 100 μL). The fluorescence signals were recorded for 30 min in a 96-well black microplate at $\lambda_{\text{ex}}/\lambda_{\text{em}} = 485 \text{ nm}/520 \text{ nm}$.

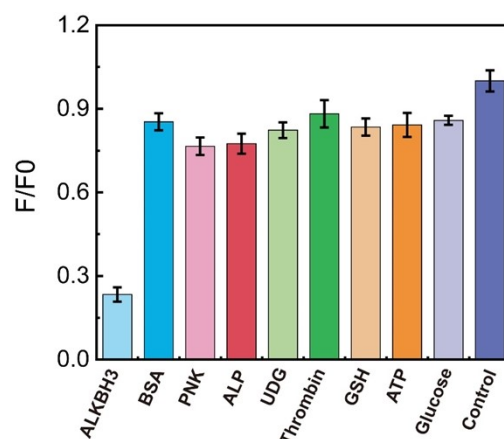


Fig. S11. Fluorescence response of RCD1T/S^{m1A} under the treatment with ALKBH3 (250 nM), BSA (5 µg/mL), PNK (20 U/mL), ALP (2 U/mL), UDG (5 U/mL), thrombin (1.8 nM), GSH (100 µM), ATP (5 mM), and glucose (200 µM). The error bars represent standard deviations of three independent experiments.

Experimental details: The protocol was similar to the one described in **Fig. S7** except that: BSA (5 µg/mL), PNK (20 U/mL), ALP (2 U/mL), UDG (5 U/mL), thrombin (1.8 nM), GSH (100 µM), ATP (5 mM), and glucose (200 µM) were used.

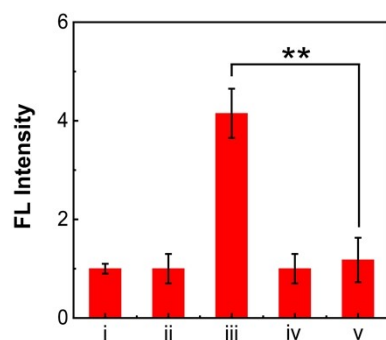


Fig. S12. The acquired fluorescence distribution of HUHS015-pretreated PC-3 cells under different conditions as indicated: i) PC-3 with S^{m1A} , ii) PC-3 with RCD1T/ S^{m1A} , iii) PC-3 with RCD1T/ S^{m1A} and Mn^{2+} , iv) PC-3 with RCD1TM/ S^{m1A} and Mn^{2+} , v) PC-3 with RCD1T/ S^A and Mn^{2+} . Data are expressed as mean \pm SD of three biological replicates. ****** $P < 0.01$ (one-way ANOVA followed by Tukey's multiple comparisons test).

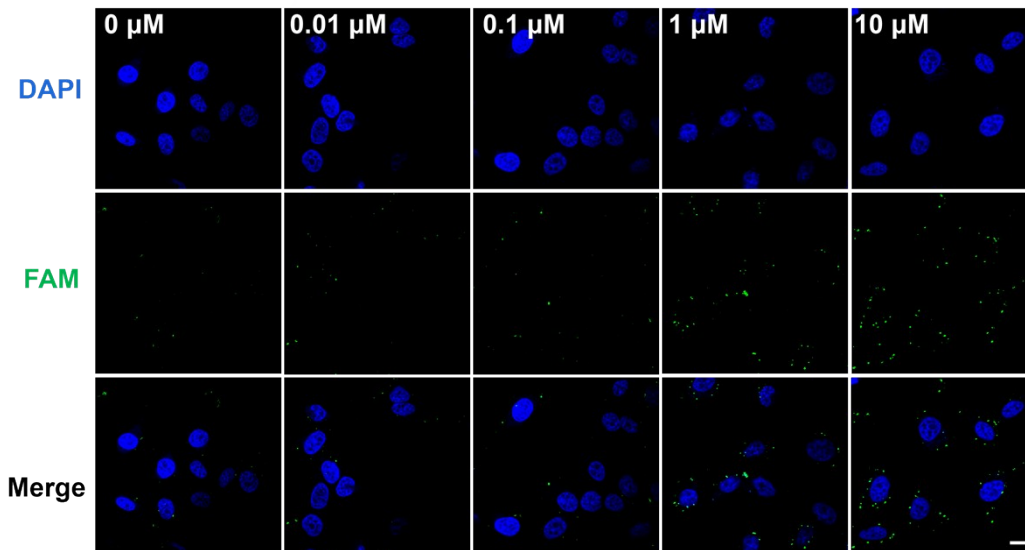


Fig. S13. Confocal fluorescence imaging of RCD1T/S^{m1A} system in response to different concentrations of HUHS015 (0, 0.01, 0.1, 1, and 10 μM). The cell nuclei were stained in blue by DAPI. Scale bar: 20 μm .

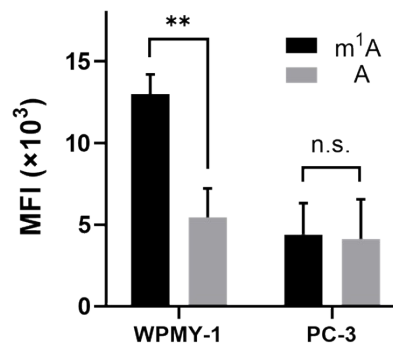


Fig. S14. The histogram of the mean fluorescence intensity (MFI) of at least 10,000 cells by flow cytometry analysis. Error bars represent the SD from three biological replicates. n.s. not significant, ** $P < 0.01$ (two-way ANOVA followed by Sidak's multiple comparisons post-test).

Uncropped gel images

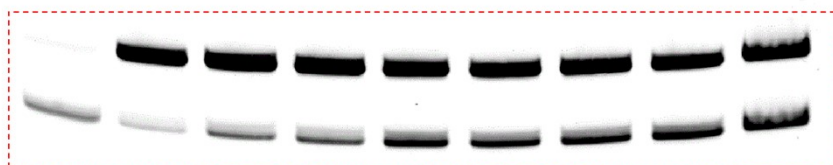


Figure 2a (top)

Uncropped PAGE gel for Figure 2a (top). The red box indicates the region presented in Figure 2a (top).

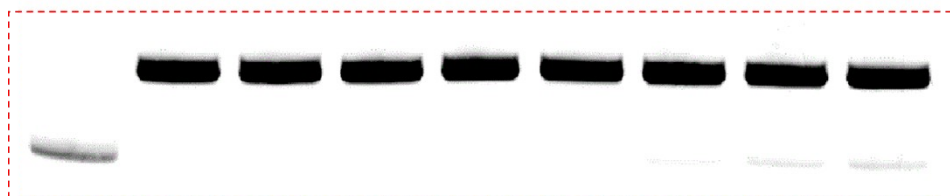


Figure 2a (bottom)

Uncropped PAGE gel for Figure 2a (bottom). The red box indicates the region presented in Figure 2a (bottom).

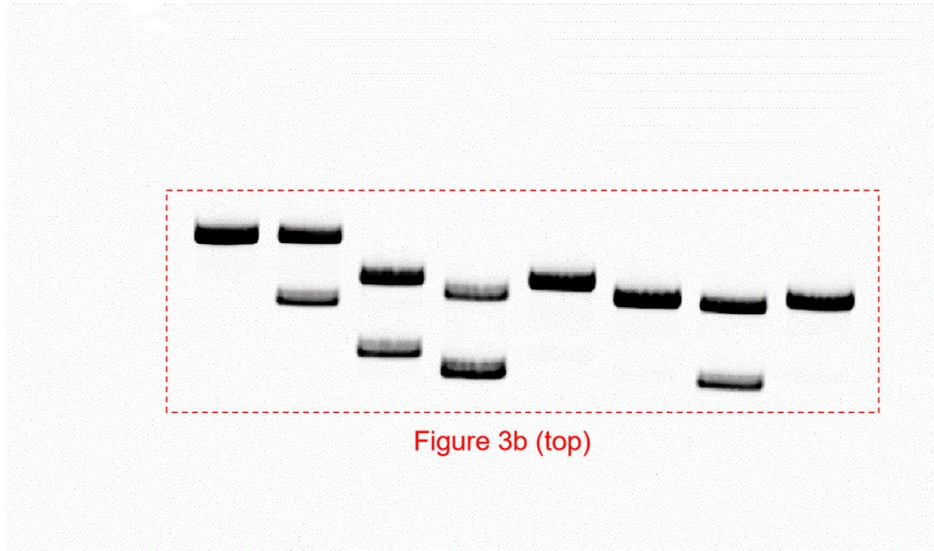


Figure 3b (top)

Uncropped PAGE gel for Figure 3b (top). The red box indicates the region presented in Figure 3b (top).

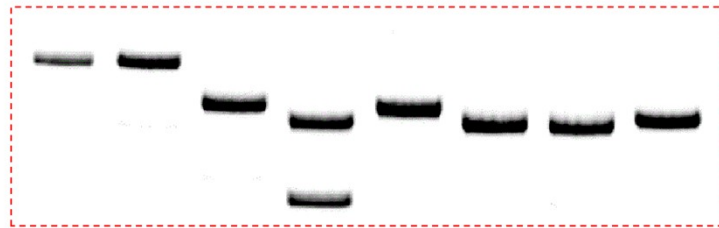
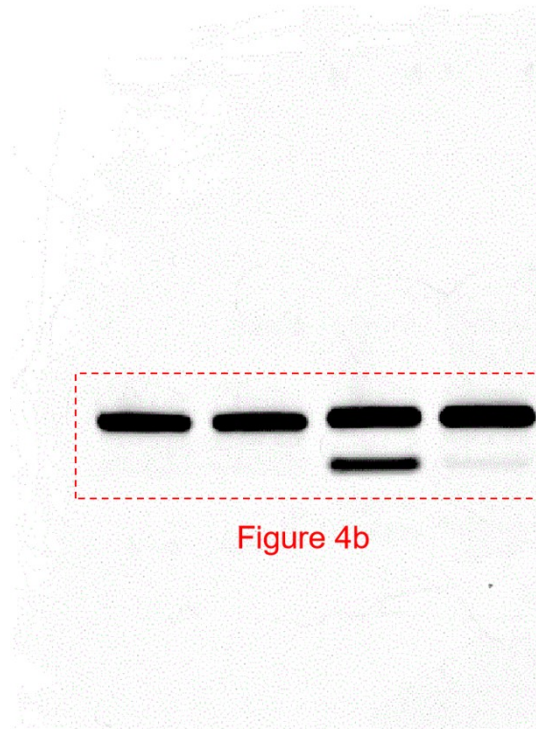
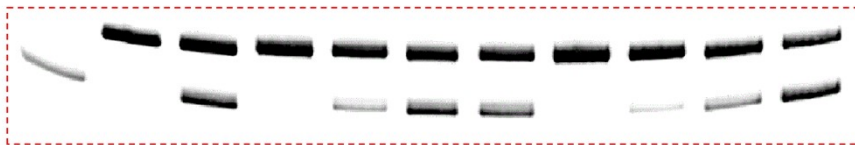


Figure 3b (bottom)

Uncropped PAGE gel for Figure 3b (bottom). The red box indicates the region presented in Figure 3b (bottom).



Uncropped PAGE gel for Figure 4b. The red box indicates the region presented in Figure 4b.



Uncropped PAGE gel for Figure S1. The red box indicates the region presented in Figure S1.



Figure S2

Uncropped PAGE gel for Figure S2. The red box indicates the region presented in Figure S2.

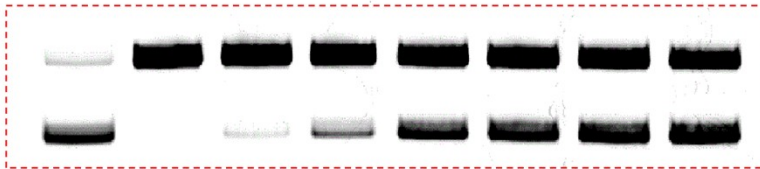


Figure S3

Uncropped PAGE gel for Figure S3. The red box indicates the region presented in Figure S3.

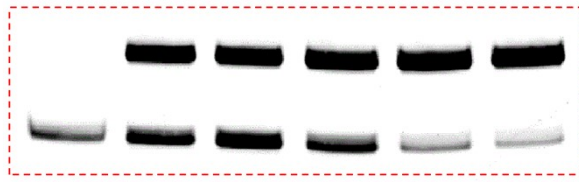


Figure S4

Uncropped PAGE gel for Figure S4. The red box indicates the region presented in Figure S4.

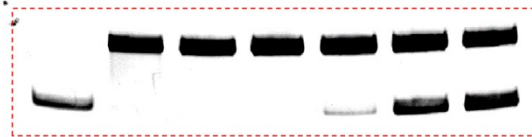


Figure S5 (top)

Uncropped PAGE gel for Figure S5 (top). The red box indicates the region presented in Figure S5 (top).

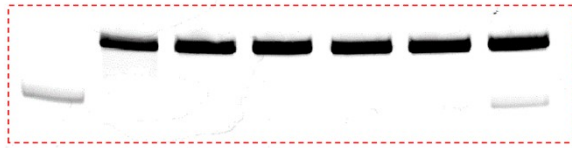


Figure S5 (bottom)

Uncropped PAGE gel for Figure S5 (bottom). The red box indicates the region presented in Figure S5 (bottom).

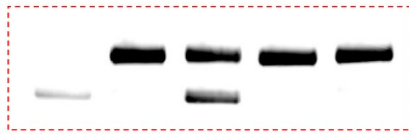


Figure S6

Uncropped PAGE gel for Figure S6. The red box indicates the region presented in Figure S6.



Figure S7

Uncropped PAGE gel for Figure S7. The red box indicates the region presented in Figure S7.



Figure S8 (top)

Uncropped PAGE gel for Figure S8 (top). The red box indicates the region presented in Figure S8 (top).

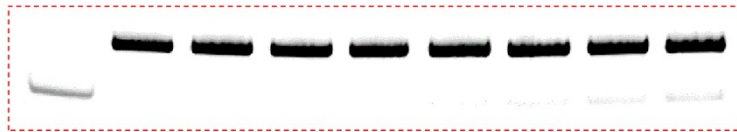


Figure S8 (bottom)

Uncropped PAGE gel for Figure S8 (bottom). The red box indicates the region presented in Figure S8 (bottom).