Supporting Information

Scheme S1. The synthetic routes of Biotin-labeled PDC.

Table S1. Characteristics of the putative G4s in STING promoter.

Table S2. Name and sequence of the oligonucleotides and primers used in this study.

Figure S1. The sequencing result of the two sgRNA plasmids (sg1 and sg2).

Figure S2. Cytotoxicity of Bio-PDC against HEK293T cells

Figure S3. Sequence of the modified PX330 Vector.

Figure S4. The inhibition of STING expression in HEK293T cells without sgRNA.

Figure S5. The construction of the luciferase reporter system reporter system.

Figure S6. Normalized luciferase activity on reporter plasmid with or without CRISPR-PDC system.

Figure S7. Correlation analysis between the expression of STING and TP53 in different brain regions by GEPIA database.

Figure S8. Correlation analysis between STING and TP53 in whole brain by GEPIA database.

Figure S9. The mRNA levels of STING treated with or without CRISPR-PDC system.

Figure S10. The mRNA levels of KRAS treated with or without CRISPR-PDC system.

Figure S11. The mRNA levels of cKIT treated with or without CRISPR-PDC system.

Figure S12. The mRNA levels of HRAS treated with or without CRISPR-PDC system.

Figure S13. The mRNA levels of HIF1-α treated with or without CRISPR-PDC system.

Figure S14. Representative SA-β-gal staining in different conditions in HMC3 microglia cells.

Figure S15. The inhibition of STING by siRNA.

Figure S16. Visualization of Aβ internalization by CLSM in vehicle or CRISPR-PDC system-treated senescent HMC3 cells.

Figure S17. Verification of G4 structure formation in the TBK1 and IRF3 promoter region.

Figure S18. Un-cropped native polyacrylamide gel electrophoresis images of Figure 2B.

Figure S19. Un-cropped western blotting images of Figure 3D.

Figure S20. Un-cropped western blotting images of Figure 3F.

Figure S21. Un-cropped western blotting images of Figure 3H.

Figure S22. Un-cropped western blotting images of Figure 5B.

Figure S23. Un-cropped western blotting images of Figure S4.

Figure S24. Un-cropped western blotting images of Figure S15.

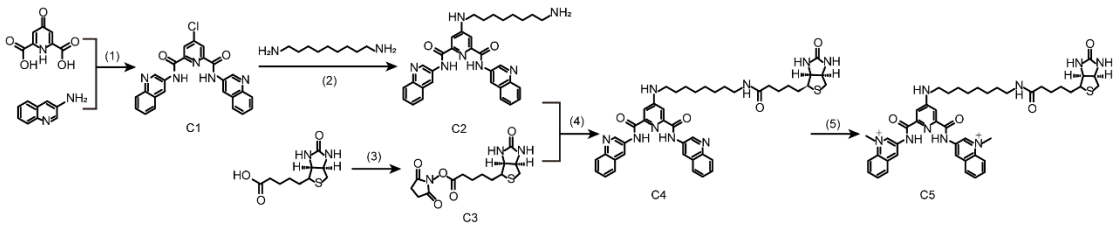
Materials and Methods

Chemical and materials

Oligonucleotides were ordered from Sangon Biological Engineering Technology & Services (Shanghai, China) and GENEWIZ Biotechnology Co., Ltd(Suzhou, China). Pyrido Dicarboxamide (PDC) and Etoposide were obtained from MCE. Fluorescein 5-isothiocyanate (FITC)-Aβ (>95%) were customized from NovoPep Limited (Shanghai, China). All chemicals were used as supplied. All water used to prepare buffer solutions was obtained by using a Milli-Q water system.

Methods

The synthetic routes of Biotin-labeled PDC.



C1:4-Chloro-N²,N⁶-bis(3-quinolyl)pyridine-2,6-dicarboxamide
C2:4-((8-aminooctyl)amino)-N²,N⁶-di(quinolin-3-yl)pyridine-2,6-dicarboxamide
C3:Biotin N-hydroxysuccinimide ester
C4:4-((8-(5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamido)octyl)amino)-N²,N⁶-di(quinolin-3-yl)pyridine-2,6-dicarboxamide
C5:3,3'-((4-((8-(5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamido)octyl)amino)pyridine-2,6-dicarbonyl)bis(azanediyl))bis(1-methylquinolin-1-ium) (Biotin-labeled Pyrido Dicarboxamide (Bio-PDC))

Scheme S1. The synthetic routes of Bio-PDC.

(1) Synthesis of C1(Compound 1)

Under argon atmosphere, dry DMF (0.35 mL, 9.00 mmol) was added dropwise to a suspension of vacuum-dried chelidamic acid monohydrate (2.01 g, 9.94 mmol) in $SOCl_2$ (25 mL). The mixture was stirred under reflux for 24 h. The volatiles were removed in vacuo, giving the crude 4-chloropyridine-2,6-dicarbonyl chloride as an off-white solid. This intermediate was dissolved in dry DMF (10 mL) and added in small portions, within 45 min, to a mixture of 3-aminoquinoline (3.16 g, 21.9 mmol) and triethylamine (3.05 mL, 21.9 mmol) in dry DMF (20 mL), stirred in an ice bath. The mixture was stirred at room temperature for 4 h and poured into water (200 mL). The white solid was collected by filtration, thoroughly washed with water and dried in vacuo, to give compound **1** (2.36 g, 52%) as a white solid. δ_H (400 MHz, DMSO-d_6) 11.48 (1 H, s), 9.37 (1 H, d, *J* 2.5), 8.99 (1 H, d, *J* 2.5), 8.49 (1 H, s), 8.11 – 8.04 (2 H, m), 7.75 (1 H, ddd, *J* 8.4, 6.9, 1.6), 7.66 (1 H, ddd, *J* 8.1, 6.9, 1.3). MS (ESI-MS): m/z= 453.9 $[M+H]^+$.

(2) Synthesis of C2(Compound 2)

In a 25 ml flask, 4-chloro-N^2, N^6-di(quinolin-3-yl) pyridine-2,6dicarboxamide **1** (0.79 g, 1.74 mmol), octane-1,8-diamine (3.6 g, 25 mmol) and triethylamine (0.5 ml) were suspended in DMSO (5 ml). The suspension was warmed to 100°C (octane-1,8-diamine dissolved at roughly 50°C) and the mixture was stirred overnight. The solution became clear. After cooling, H_2O was added (60 ml) and the precipitate was filtered and washed with water (300 ml). The solid was dried under vacuum affording compound **3** (1.838 g, 94 % yield) as a pale yellow powder. δ_H (400 MHz, DMSO-d_6) 9.36 (2 H, d, *J* 2.5), 8.96 (2 H, d, *J* 2.5), 8.05 (2 H, dd, *J* 4.2, 1.3), 8.03 – 8.01 (2 H, m),

7.72 (2 H, ddd, *J* 8.3, 6.8, 1.5), 7.63 (2 H, ddd, *J* 8.1, 6.8, 1.3), 7.56 – 7.47 (2 H, m), 3.23 (2 H, d, *J* 5.8), 1.60 (2 H, q, *J* 7.2), 1.41 – 1.27 (16 H, m). MS (ESI-MS): m/z= 562.5 $[M+H]^+$.

(3) Synthesis of C3(Compound 3)

A 50 mL-round bottom flask containing D-biotin (1.2 g, 5 mmol) was heated to dissolve in DMF (10 mL). The solution was cooled to room temperature, and N-hydroxysuccinimide (0.575 g, 5 mmol) and dicyclohexylcarbodiimide (1.24 g, 6.5 mmol) were added. After stirring at room temperature overnight, white precipitation was filtered. The filtrate was evaporated, stirred in ether, and filtered to obtain the title compound as a white solid (100%). δ_H (400 MHz, DMSO-d_6) 6.41 (1H, s), 6.35 (1H, s), 4.33−4.28 (1H, m), 4.16−4.13 (1H, m), 3.14−3.06 (1H, m), 2.86−2.78 (4H, m), 2.73− 2.65 (2H, m), 2.58 (1H, d), 1.70−1.36 (6H, m). MS (ESI-MS): m/z= 342.4 $[M+H]^+$.

(4) Synthesis of C4(Compound 4)

4-((8-aminooctyl) amino)-N^2, N^6-di(quinolin-3-yl) pyridine-2,6-dicarboxamide **2**, Biotin N-hydroxysuccinimide ester **3** in DMF (5 ml) and triethylamine was added to a 25 ml flask. After stirring at room temperature overnight, H_2O was added (45 ml) and the precipitate was filtered and washed with water. The solid was dried under vacuum affording intermediate **4**.

(5) Synthesis of C5(Compound 5, Biotin-labeled PDC)

A solution of intermediate **4** (19.7mg, 0.25 mmol) and iodomethane (1.56 mL, 3.55 g, 25 mmol) in freshly distilled DMF (2.5 mL) was stirred in a sealed tube at 40 °C for 24 h. After cooling to room temperature, the suspension was poured into acetone (10 mL). The precipitate was collected by centrifugation, washed with acetone and Et_2O (2 × 10 mL), and dried in vacuo. The crude product was additionally recrystallized from MeOH to obtain compound **5**. δ_H (400 MHz, DMSO-d_6) 11.79 (2 H, s), 10.11 (2 H, d, J 2.5), 9.64 (2 H, s), 8.53 (4 H, d, J 7.9), 8.23 (2 H, t, J 8.0), 8.08 (2 H, t, J 7.6), 7.82 – 7.76 (1 H, m), 7.68 (1 H, s), 6.45 – 6.31 (1 H, m), 4.77 (6 H, s), 4.17 – 3.98 (2 H, m), 2.88 (2 H, s), 2.56 (4 H, t, J 5.5), 2.07 (2 H, dt, J 18.9, 7.3), 1.62 (2 H, d, J 7.6), 1.41 – 1.27 (18 H, d, J 43.9). MS (ESI-MS): m/z= 818.8 $[M]^{2+}$.

Bioinformatics analysis

The promoter sequences of STING were retrieved from the NCBI Genome database (https://www.ncbi.nlm.nih.gov/genomes). The FASTA sequences of the promoter of STING were then used for the prediction of the putative G4-forming sequences (PQSs) with QGRS-mapper[1], Pqsfinder[2]and G4Hunter[3] (G4H). The integration of these three methods is conducive to enhance the precision in identifying stable G4 structures, thereby contributing to a more accurate prediction of PQSs.

QGRS Mapper can predict and score putative quadruplex forming G-rich sequences (QGRS) based on the folding rule,which consider sequences that match the sequence formula perfectly. Shorter loops, G-quadruplexes have loops roughly equal in size and the greater the number of guanine tetrads will result in higher scores,which indicates that the QGRS sequence is more likely to form G4.

Pqsfinder is a imperfection-tolerant QGRS search tool which allows mismatches or bulges. After identifying potential QGRS sequences, it examines the potential of such G runs to form a stable G4 and reports a corresponding quantitative score. The scoring scheme was designed to quantitatively approximate the relationship between G4 sequence and the stability of its structure.

The higher the score, the greater the probability of stable G4 formation.
G4H defined a scoring function that reflects G4 propensity, rather than defining an arbitrary limit on the number of consecutive guanines required or on loop size. It attributes an increasing positive score to each contiguous G and a negative counterpart for contiguous C. The sequence is scored by the average of the values and the score is positively correlated with G4 forming propensity.
The Pqsfinder (https://pqsfinder.fi.muni.cz/), QGRS-mapper (https://bioinformatics.ramapo.edu/QGRS/analyze.php), and G4Hunter (https://bioinformatics.cruk.cam.ac.uk/G4Hunter/) were run by their online tools.

Native polyacrylamide gel electrophoresis analysis

Native gel electrophoresis was carried out on acrylamide gel (20 %) and was silver stained. To prepare the final sample, the oligonucleotides were heated at 95 °C for 5 min, and then slowly cooled to room temperature in 100 mM K^+.

Fluorescence measurements of NMM

The assays were carried out on a JASCO FP-6500 spectrofluorometer at 25 °C.Briefly, fluorescence samples (400 μL), containing NMM (2 μM), DNA strand (1 μM) and metal ions (K^+) of 100 mM concentration were incubated for 1.5 h at 4 °C, and mixtures emission spectra were tested on a JASCO FP-6500 spectrofluorometer on 399 excitation wavelength at 20 °C.

Circular dichroism (CD) spectroscopy measurements

CD spectra experiments were carried out on a JASCO J-810 spectropolarimeter. The optical chamber of CD spectrometer was deoxygenated with dry purified nitrogen (99.99%) for 45 min before use, and kept the nitrogen atmosphere during experiments. CD samples, containing DNA strands (15 μM) and metal ions (K^+) of 100 mM concentration were heated at 95 °C for 5 min, slowly cooled down to room temperature, incubated overnight and then tested on a JASCO J-810 spectropolarimeter.

NMR spectroscopy

^{1}H NMR spectrum was recorded on a Bruker-600 MHz NMR instrument. The lyophilized DNA samples were dissolved in a 25 mM phosphate-buffered saline solution (pH 7.0) with 100 mM K+ and 10% D2O, resulting in a final concentration of 1.0 mM. The test was performed after incubating overnight at 4 °C.

Stopped-flow experiments

Fluorescence stopped-flow experiments were carried out by using an SX20 Stopped-Flow Spectrometer. In the assays, DNA samples (FT-STING-WT in 10 mM Tris-HCl buffer, 0 mM K^+) were mixed with K^+-containing buffer (10 mM Tris-HCl buffer, 200 mM K^+). Fluorescence changes were monitored with an emission wavelength of 515 nm at 20 °C.

Chromatin immunoprecipitation assays

For ChIP assays of BG4, it was performed as described previously[4]. Briefly,cells were fixed in 1% formaldehyde for 10 min and quenched with 0.125 M glycine. Chromatin was sonicated to shear to an average size of 100–500 bp and then incubated in the presence of BG4. Anti-Flag Magnetic Beads (P2115; Beyotime) were used to capture BG4–G4 complexes. After de-crosslinking, samples were purified with the MinElute PCR Purification Kit (28006; Qiagen). G4 enrichment was quantified by performing qRT-PCR, using BeyoFast SYBR Green qPCR Mix, with the qTOWER2.0 quantitative real-time PCR system. The primers used for ChIP assays are provided in Supplementary Table 2.

UV melting

A Cary 300 UV/Vis spectrophotometer was used for melting curves collect ion and analysis. For sample preparation, DNA (2μM) and ligands(3μM) were mixed in a solution containing 100mM K^+ and then incubated overnight at 4° .UV melting performed absorbance changes of melting samples at 295 nm versus temperature at a heating rate of 1 °C /min with the same concentration of ligands solution as the reference solution.

Vectors construction

The STING promoter sequence were inserted into the pGL3-Basic vector (Promega,USA) between KpnI and XmaI restriction enzyme sites at the 5′ end of the luciferase gene by genewiz(China).
The sgRNA expression plasmid and dcas9-mSA plasmid were obtained as described[5].
The overexpression plasmid of TP53, siRNA-TP53 and siRNA-STING were bought from Geneppl technology, co, Ltd (Nanjing,China).

Cell culture

The human embryonic kidney cell line HEK293T were a generous gift from Dr. Qian Jin (Beijing Institute of Lifeomics, Beijing, China). The human microglia HMC3 were purchased from Servicebio LTD(Servicebio,Wuhan,China). All these cell lines were maintained in high-glucose Dulbecco's modified Eagle's medium (DMEM; Gibco, USA) supplemented with 10% fetal bovine serum (FBS; Kang Yuan Biology, China). The cells were incubated at 37 °C in a humidified incubator containing 5% CO_2.

Transfection of plasmids and siRNA

Lipofectamine 2000 reagent (Invitrogen) was used for transfections of plasmids and siRNA, according to the manufacturer's instructions. Briefly, cells were seeded to 70% confluence at the time of transfection. Plasmids/siRNA and Lipofectamine 2000 were mixed in DMEM without serum. The mixtures were incubated for 15 min at room temperature and added to cells in each

dish. After 7h, the cells were treated with fresh medium with or without the Bio-PDC(1μM) and were collected at the indicated times.

Cell Toxicity Assay

For the CCK-8 assay, cells were plated at a density of 5000 cells per well on 96-well plates overnight. After incubation of 24 h, different final concentrations of Bio-PDC were added to the cells (Final concentration: C(Bio-PDC) = 0,0.1, 0.5, 1.0, 1.5, 2.0, 4.0, 6.0, 8.0, 10.0 μM). 48 h later, 100 μL of tenfold diluted CCK-8 solution was used to replace the mixture in each well and the cells were further incubated for another 4 h. Absorbance values were measured at 465 nm using Microplate reader (CLARIOstar Plus,BMG LABTECH,Germany).

Real-time quantitative polymerase chain reaction (RT-qPCR) assays

Total RNAs were extracted from cultured cells or tissues using RNApure tissue&cell kit (CWBIO, China) according to the manufacturer's protocol. The cDNAs were synthesized from 500 ng of total RNAs using PrimeScript RT reagent kit (Takara, Japan) according to the manufacturer's protocol. The RT-qPCR assays were performed using SYBR FAST qPCR kit (Beyotime, China) at the Jena real-time PCR system (Analytikjena, Germany), with GAPDH as the internal control. The relative expression levels of RNAs were calculated using the comparative Ct method. The primer sequences for RT-qPCR are listed in Table S2.

Western blotting assays

For protein analysis of whole-cell lysates, cells were lysed in RIPA (CWBIO, Beijing, China) buffer. After electrophoresed on SDS-polyacrylamide gels, proteins were transferred to nitrocellulose filter (NC) membranes and then blocked in 5% skim milk diluted with TBST solution. After an incubation with antibodies specific (AG5348(STING); AF1162(TP53); AF1594(p-IRF3); AF2458(IRF3), Beyotime, Shanghai, China;72971(p-STING), Cell Signaling Technology,USA) or β-Tubulin (AF2839; Beyotime, Shanghai, China), the blots were incubated with anti-rabbit (#CW0103M; CWBIO, Beijing, China) secondary antibodies conjugated to horseradish peroxidase (HRP). The immunoreactive bands were detected using Sparkjade chemiluminescent substrate kit (Sparkjade, Shandong, China).

Luciferase reporter gene assay

When the volume of adherent cells occupied 70% of the 96-well plates (Servicebio,Wuhan,China), the plasmids were transfected into cells using Lipofectamine 2000 (Invitrogen, USA), following the manufacturer's instructions. Media was changed after 7 h post-transfection and cells were treated with Bio-PDC (1μM) or vehicle (distilled water) for 48 h. (If not otherwise indicated, cell transfection and drug treatment for the following experiments were performed in this manner).Luminescence intensity was measured using the Bio-Lumi™ firefly luciferase reporter gene detection kit (RG042S,Beyotime,Shanghai,China) by microplate reader(CLARIO star Plus, BMG LABTECH, Germany).

SA-β-Gal assay

SA-β-Gal Fix solution (SA-β-Gal staining kit, Solarbio Life Science, China) were added in plate for 15 min after washing with PBS. Subsequent SA-β-Gal work solution (SA-β-Gal staining kit, Solarbio Life Science, China) were added in plates after removal of A solution and washing with PBS three times. Samples were incubated at 37 °C for overnight. Results were observed in white light phase by inverted fluorescence microscope.

Preparation of Aβ42 Aggregates

Aβ42 was provided NovoPep Limited (Shanghai, China). The sample was prepared as previously described. Briefly, the powdered Aβ42 was dissolved in 1,1,1,3,3,3-hexafluoro-2-propanol solution (HFIP) at a concentration of 1 mg mL^{-1}. Before used, the sample was evaporated, and redissolved in anhydrous dimethyl sulfoxide (DMSO), followed by diluting to the target concentration with PBS (10×10^{-3} M, pH 7.4) buffer. Oligomers (100μM) were obtained by storage the fresh solution at 4 °C for 24 h.

Cellular Phagocytosis of Aβ

For confocal laser-scanning microscopy, the HMC3 cells were plated on the 24-well plates. For the induced senescence group,the cells were treated with complete medium containing 3μm Eto for 48h.For the treatment group, after treating with complete medium containing 3μm Eto for 48h， transfection plasmids and then the medium was replaced with complete medium at a final concentration of 1μM Bio-PDC. After 48h, the medium was changed to DMEM supplemented with 5% fetal bovine serum (FBS; Kang Yuan Biology, China) to culture for 6 h,then FITC-Aβ were added to the cells at a final concentration of 10μM. After incubation for 6 h, the cells were washed three times with PBS buffer. Then the cells were stained according to the instructions. The lyso-tracker red dye (C1046, Beyotime,Shanghai,China)) and Hoechst 33342(ab145597,Abcam,U.K.) was added before the PBS wash. Finally, subcellular localization analysis of Aβ peptides in each sample was performed using Nikon CLSM.

1 O. Kikin, L. D'Antonio and P. S. Bagga, *Nucleic Acids Res.*, 2006, **34**, W676–W682.
2 P. Agarwala, S. Pandey, K. Mapa and S. Maiti, *Biochemistry*, 2013, **52**, 1528–1538.
3 A. Bedrat, L. Lacroix and J.-L. Mergny, *Nucleic Acids Res.*, 2016, **44**, 1746–1759.
4 R. Hänsel-Hertsch, D. Beraldi, S. V. Lensing, G. Marsico, K. Zyner, A. Parry, M. Di Antonio, J. Pike, H. Kimura, M. Narita, D. Tannahill and S. Balasubramanian, *Nat. Genet.*, 2016, **48**, 1267–1272.
5 G. Qin, Z. Liu, J. Yang, X. Liao, C. Zhao, J. Ren and X. Qu, *Nat. Cell Biol.*, 2024, **26**, 1212–1224.

Table S1. Characteristics of the putative G4s in STING promoter.

PQSs	Sequences	Position	Scores		
			QGRS	Pqsfinder	G4H
1(STING-WT)	AGGGAAGGGAAGGGAAGGGAAGGGA	-1762~-1735	42	69	2
2	GGAGGCGGAGG	-1610~-1600	21	33	1.36
3	GGGAGGCTGAGGCAGG	-1582~-1567	19	27	1.25
4	GGGAGGCCAAGGCAGG	-1446~-1431	19	27	1
5	GGAGGCGGAGCTTGCGG	-1314~-1298	15	24	0.882
6	GGAGGCTGAGGCAGG	-1280~-1266	18	27	1
7	GGCGTGGTGGCGG	-1242~-1230	19	30	1.15
8	GGGAGGCCAAGGCAAATGG	-1147~-1129	18	26	0.842
9	GGGAGGCTGAGGTGGG	-976~-961	19	29	1.62
10	GGGAGGCCAAGGCAGG	-837~-822	19	27	1
11	GGGAGGCTGAGGCAGG	-374~-359	19	27	1.25
12	GGCGTGGTGGTGGG	-337~-324	19	30	1.5
13	GGGAGGCCGAGATGGGTGG	-224~-226	16	23	1.26
14	GGAATGGGGGTTTGG	-77~-63	19	27	1.87
15	GGTGGGAGAGGAGGG	-55~-41	20	29	1.8

Table S2. Name and sequence of the oligonucleotides and primers used in this study.

Name	Sequences (5'→3')
Oligonucleotides	
STING-WT	AG GGAAGGGAAG GGAAGGGAAG GGA
STING-Mut	AG AGAAGAGAAG AGAAGAGAAG AGA
TBK1-WT	GGGGAAGGGGCGGGATTTGCAGTTGCGGG
TBK1-Mut	GAGAAAGAGACGAGATTTGCAGTTGCGAG
IRF3-WT	GGGGGAGGG AGGGAGTTGGGG
IRF3-Mut	GAGAGAGAG AGAGAGTTGAGA
Bcl-2	GGGCGCGGGAGGAATTGGGCGGG
Fluorescently-labeled oligonucleotides	
FT-STING-WT	FAM-AG GGAAGGGAAGGGAAGGGAAGGGA-TAMRA
RT-qPCR primers	
H-STING-F	TTCGAACTTACAATCAGCATTACAA
H-STING-R	CTCATAGATGCTGTTGCTGTAAACC
H-CDKN2B-F	TGGCTACGAATCTTCCG
H- CDKN2B -R	CCTCCTCCACTTTGTCCT
H-$p16^{INK4a}$-F	GGGTTTTCGTGGTTCACATCC
H- $p16^{INK4a}$ -R	CTAGACGCTGGCTCCTCAGTA
H-p21-F	TGTCCGTCAGAACCCATGC
H-p21-R	AAAGTCGAAGTTCCATCGCTC
H-IP10-F	AGTGGCATTCAAGGAGTACC
H-IP10-R	TGATGGCCTTCGATTCTGGA
H-TNFα-F	CCTCTCTCTAATCAGCCCTCTG
H-TNFα-R	GAGGACCTGGGAGTAGATGAG
H-IL1β-F	ATGATGGCTTATTACAGTGGCAA
H- IL1β-R	GTCGGAGATTCGTAGCTGGA
H-IL6-F	ACTCACCTCTTCAGAACGAATTG
H-IL6-R	CCATCTTTGGAAGGTTCAGGTTG
H-FIZZ1-F	CCGTCCTCTTGCCTCCTTC
H-FIZZ1-R	CTTTTGACACTAGCACACGAGA
CHIP primers	
RPA3-F	CGGAAGTTGACAGATACAGGG
RPA3-R	GATCGCAGAAAGGTAGTCTCAG
STING-F	GCAGGAGAACTGCTTGAACC
STING-R	CTCTCTGGAAGGGGGATTTT
TMCC2-F	CCAGACACTTTGGGTGACCT
TMCC2-R	AACACCTGCTCTGCCAACTT
NFASC-F	CAGTGGGTTTGACCCCTAGA
NFASC-R	CACCTTCAGCTCCTCCTTTG

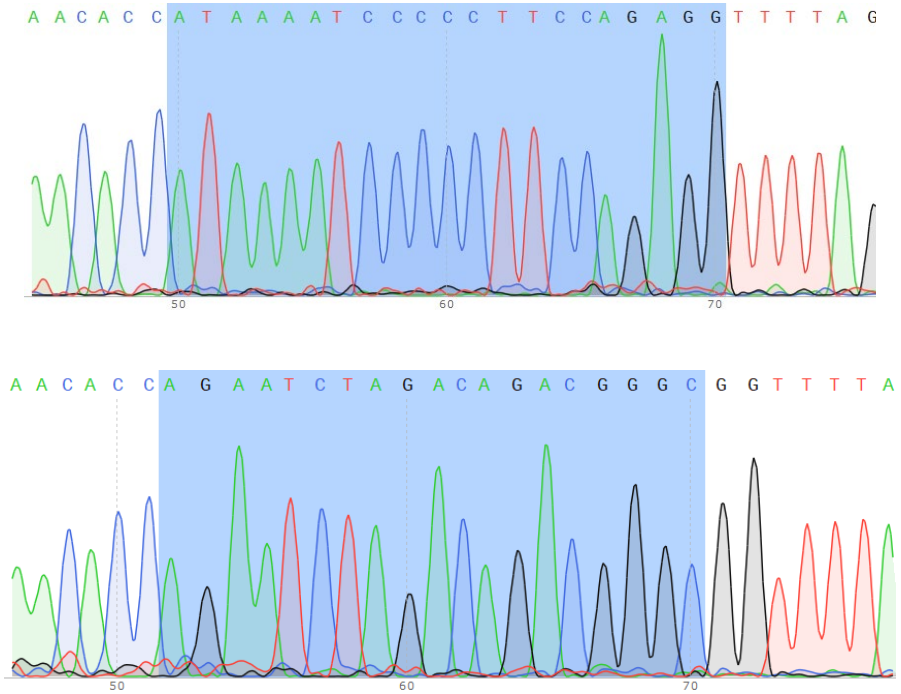


Figure S1. The sequencing result of the two sgRNA plasmids (sg1 and sg2).

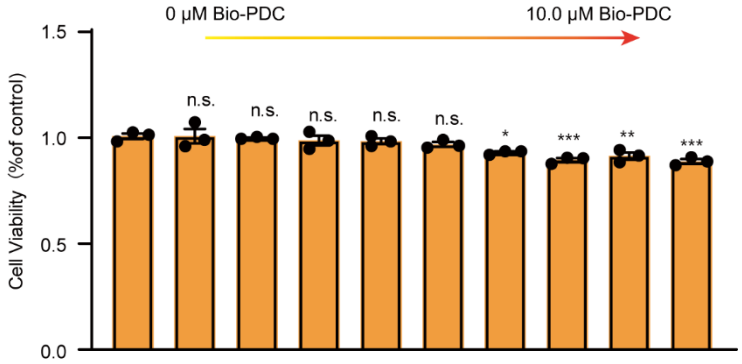


Figure S2. Cytotoxicity of Bio-PDC against HEK293T cells. The concentration of Bio-PDC was 0,0.1, 0.5, 1.0, 1.5, 2.0, 4.0, 6.0, 8.0, 10.0 μM, respectively.

GAGGGCCTATTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTTAGAGAGATAATTGGAATTAATT
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Figure S3. Sequence of the modified PX330 Vector.

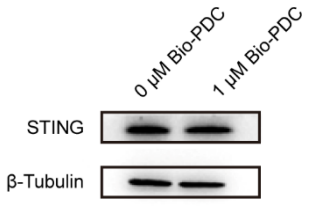

Figure S4. The inhibition of STING expression in HEK293T cells without sgRNA. The un-cropped western blotting image is shown in Figure S16.

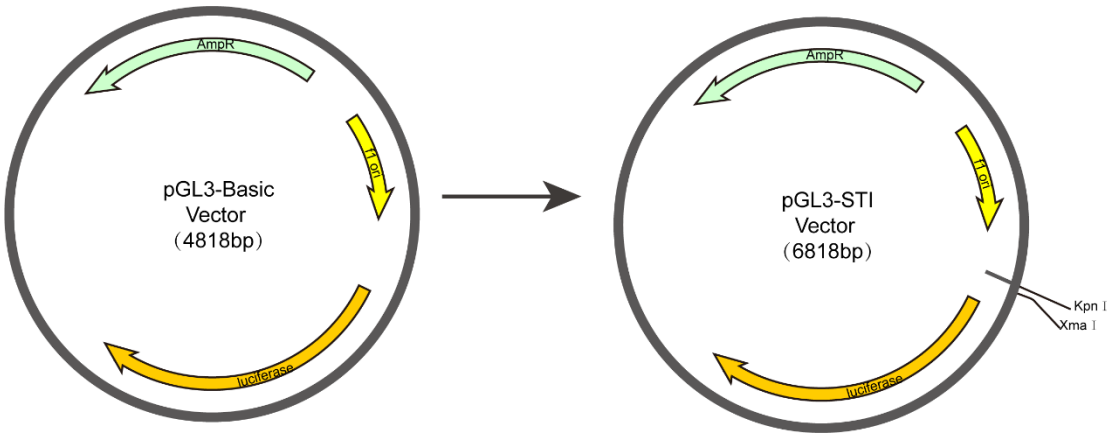

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Figure S5. The construction of the luciferase reporter system reporter system. (A) Map of the plasmid. (B) Plasmid sequence containing the STING promoter.

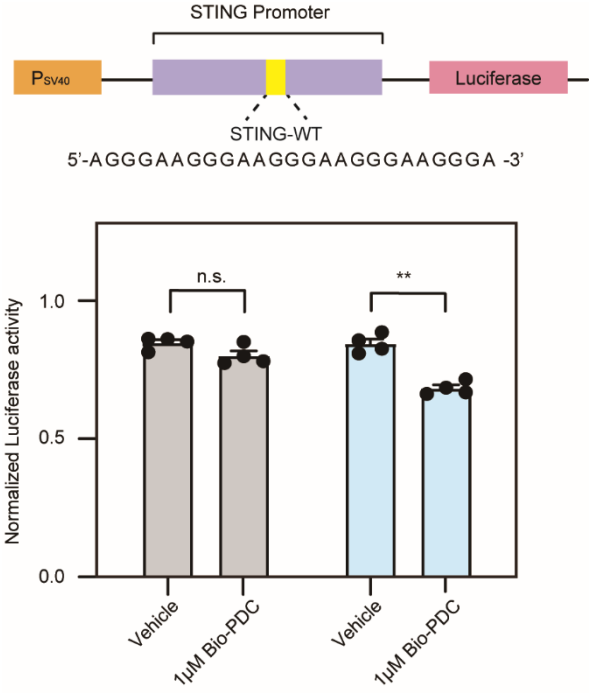

Figure S6. Normalized luciferase activity on reporter plasmid with or without CRISPR-PDC system.

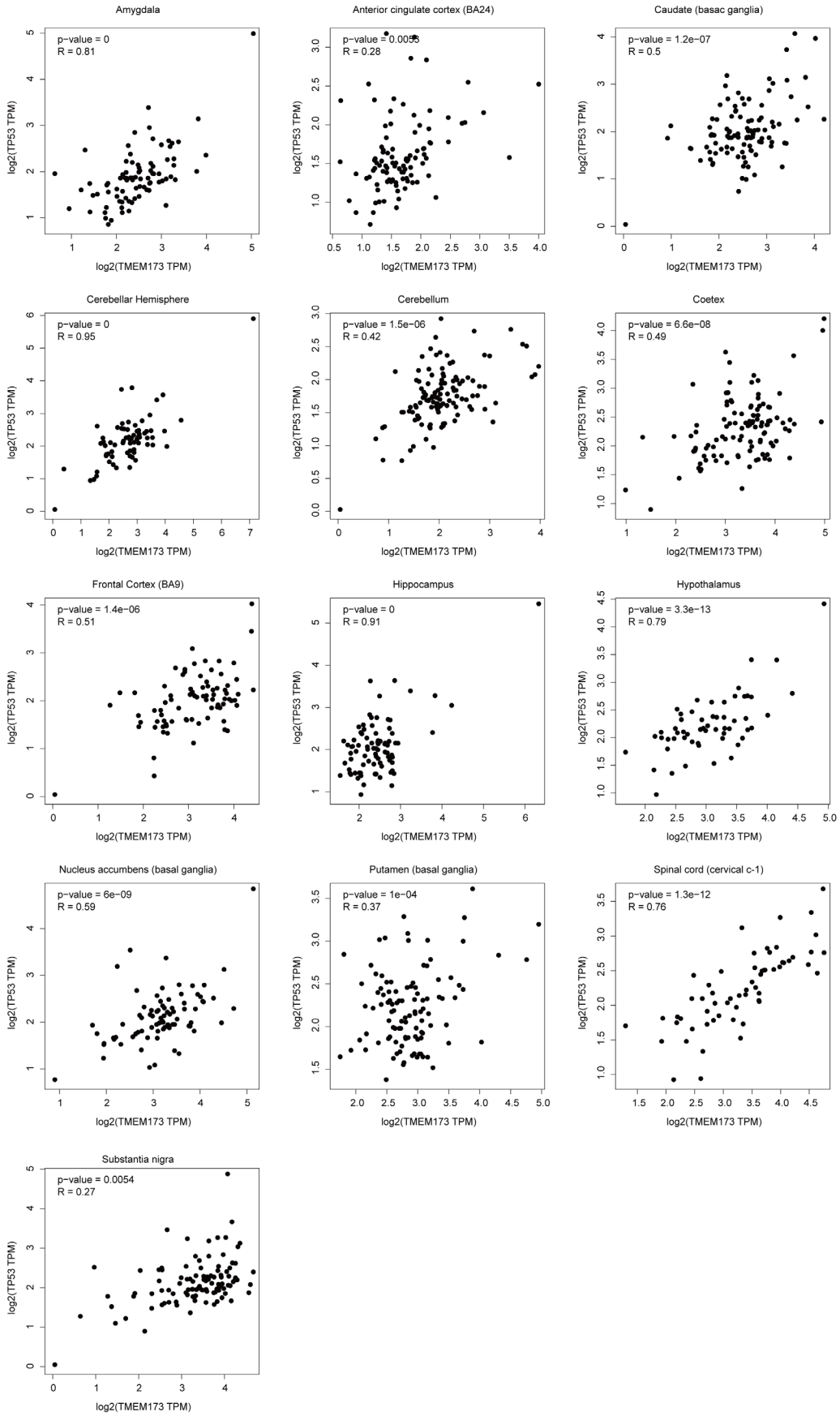

Figure S7. Correlation analysis between the expression of STING and TP53 in different brain regions by GEPIA database.

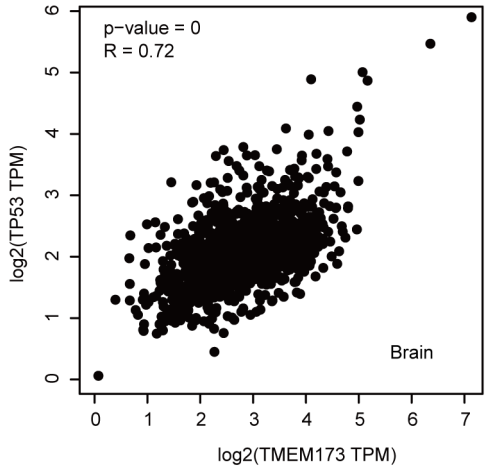

Figure S8. Correlation analysis between STING and TP53 in whole brain by GEPIA database.

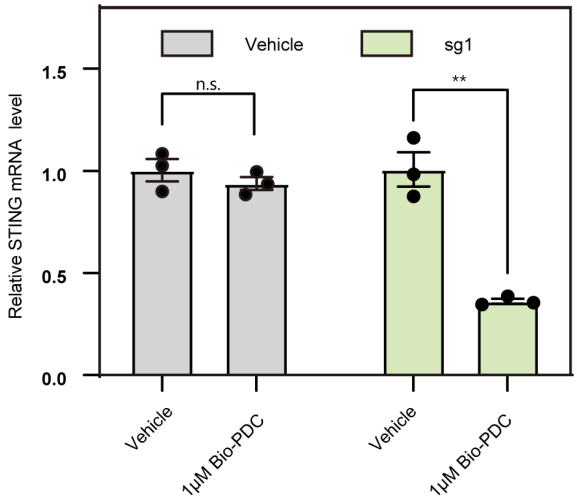

Figure S9. The mRNA levels of STING treated with or without CRISPR-PDC system, detected by RT-qPCR assays.

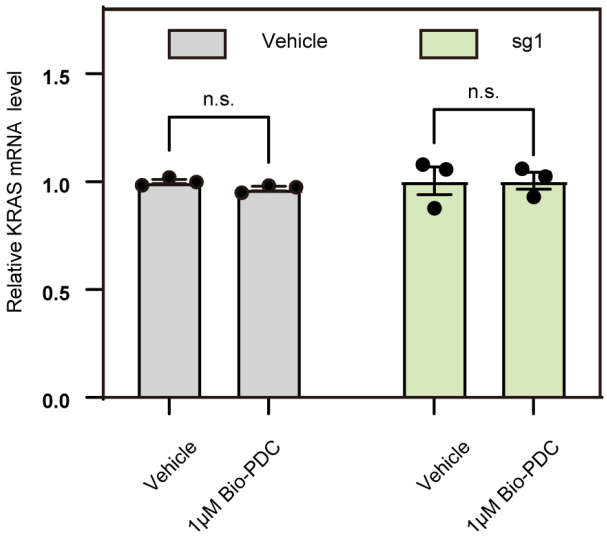

Figure S10. The mRNA levels of KRAS treated with or without CRISPR-PDC system, detected by RT-qPCR assays.

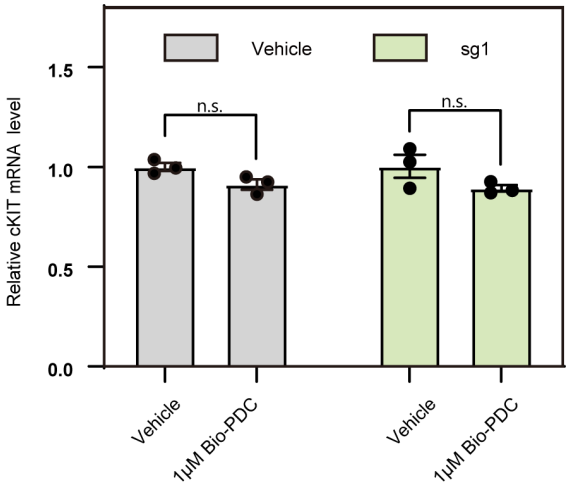

Figure S11. The mRNA levels of cKIT treated with or without CRISPR-PDC system, detected by RT-qPCR assays.

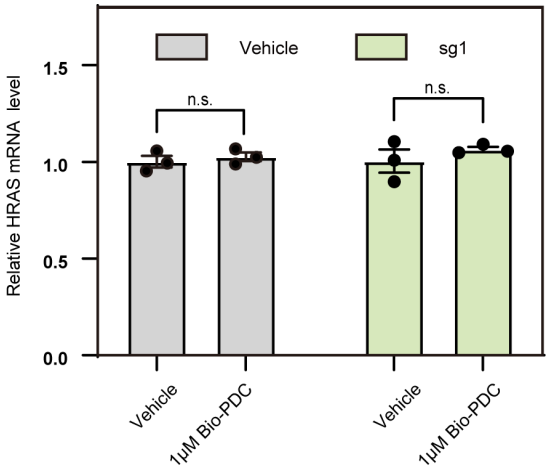

Figure S12. The mRNA levels of HRAS treated with or without CRISPR-PDC system, detected by RT-qPCR assays.

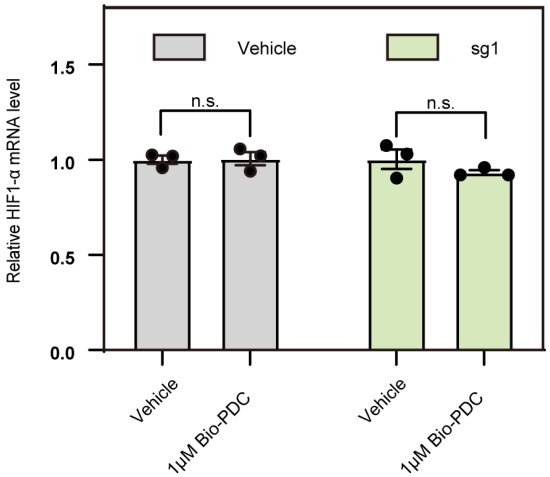

Figure S13. The mRNA levels of HIF1-α treated with or without CRISPR-PDC system, detected by RT-qPCR assays.

Figure S14. Representative SA-β-gal staining in different conditions in HMC3 microglia cells.

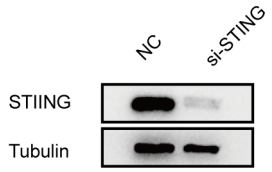

Figure S15. The inhibition of STING by siRNA.

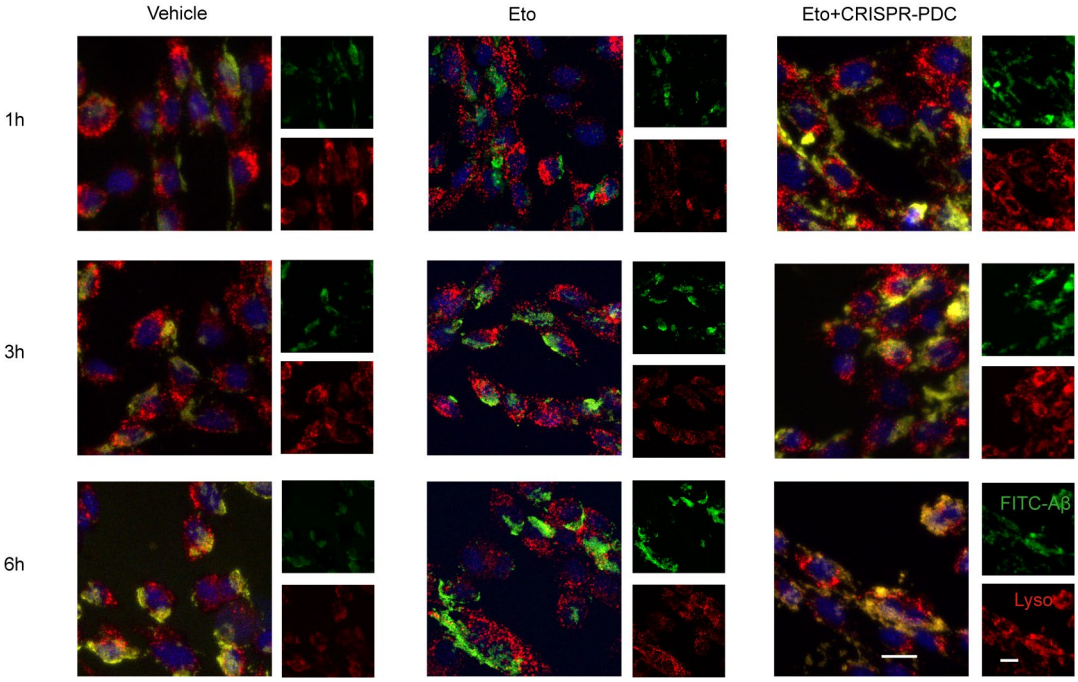

Figure S16. Visualization of Aβ internalization by CLSM in vehicle or CRISPR-PDC system-treated senescent HMC3 cells. Scale bar = 50 μm.

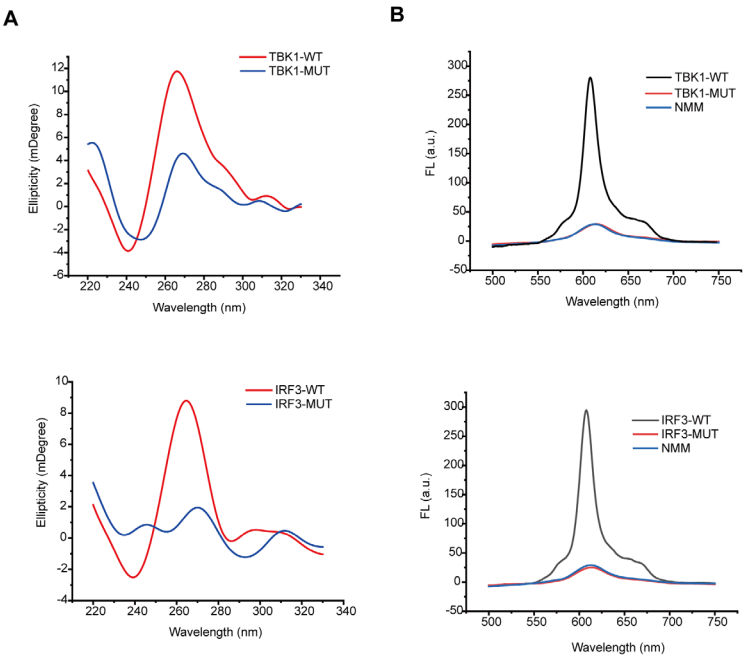

Figure S17. Verification of G4 structure formation in the TBK1 and IRF3 promoter region. (A) CD spectra of TBK1-WT (15 μM), IRF3-WT (15 μM) and their mutants (15 μM) under 100 mM K^+. (B) Fluorescence turn-on assays of TBK1-WT, IRF3-WT and their mutants. DNA samples (1 μM) were mixed with NMM (2 μM) under 100 mM K+.

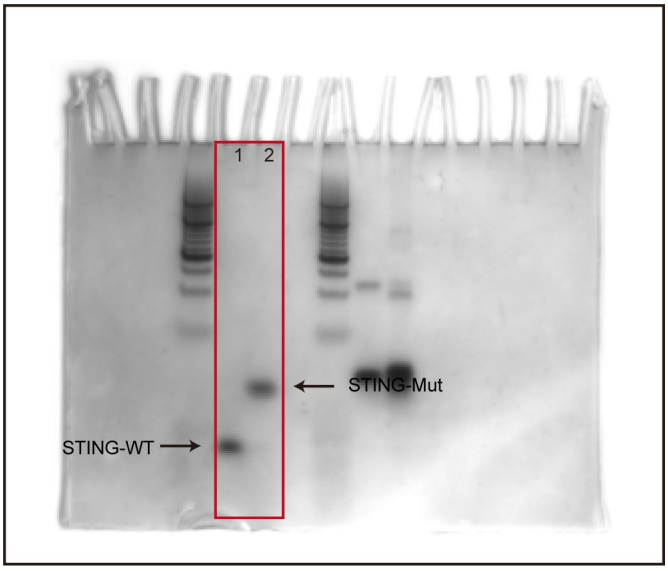

Figure S18. Un-cropped native polyacrylamide gel electrophoresis images of Figure 2B.

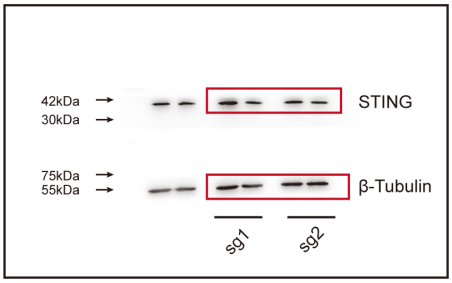

Figure S19. Un-cropped western blotting images of Figure 3D.

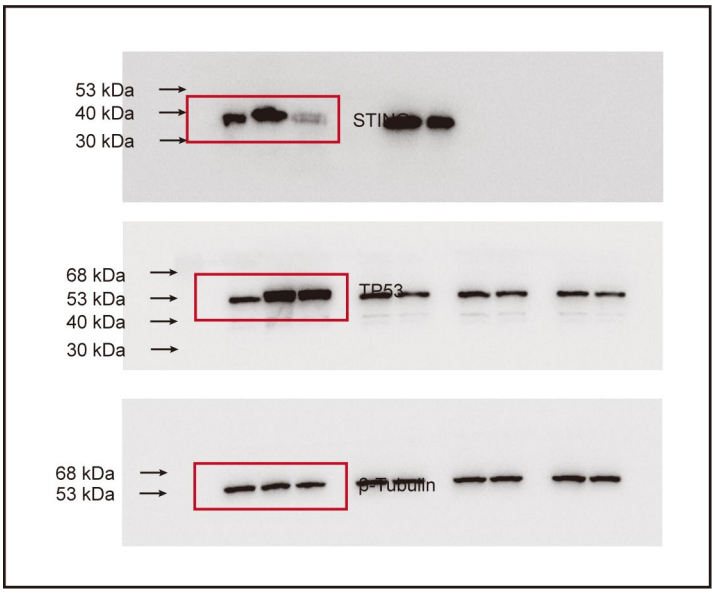

Figure S20. Un-cropped western blotting images of Figure 3F.

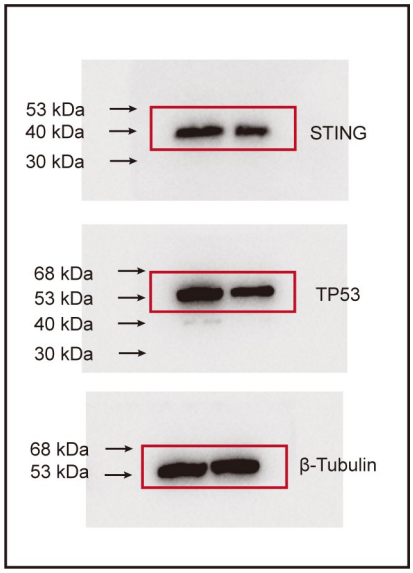

Figure S21. Un-cropped western blotting images of Figure 3H.

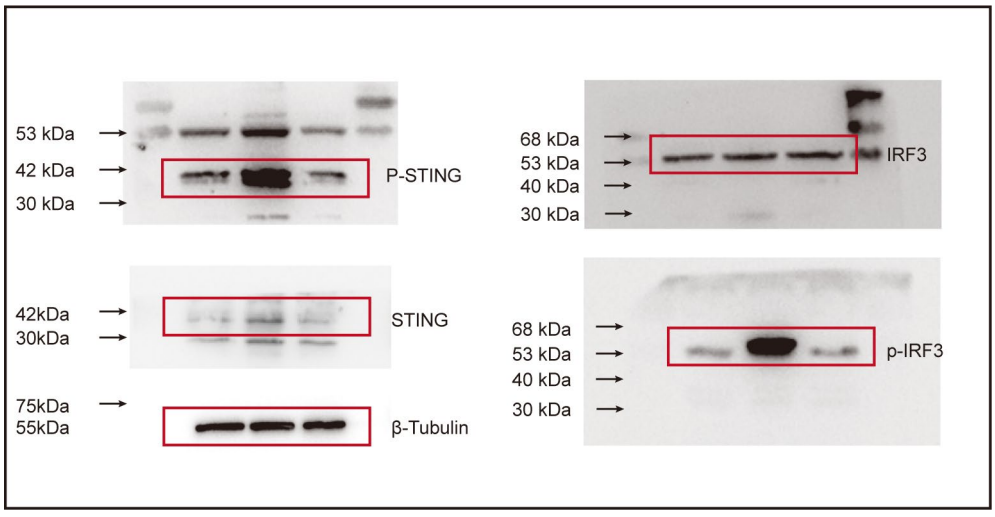

Figure S22. Un-cropped western blotting images of Figure 5B.

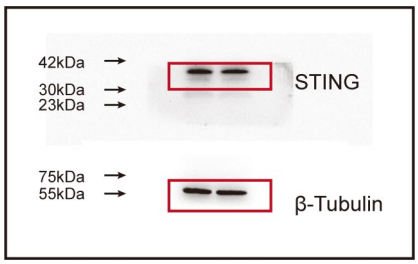

Figure S23. Un-cropped western blotting images of Figure S4.

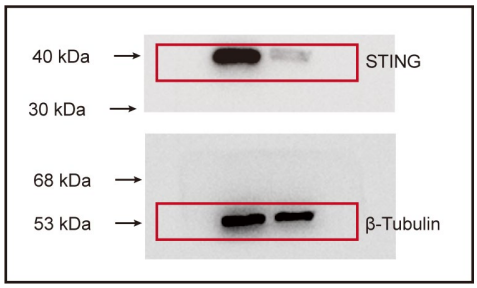

Figure S24. Un-cropped western blotting images of Figure S15.