Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.


# Supporting information

# An ultra pH-responsive peptide nanocarrier for cancer gene therapy

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## S-I Supporting data

## S-II Peptide sequences

## S-I Supporting data

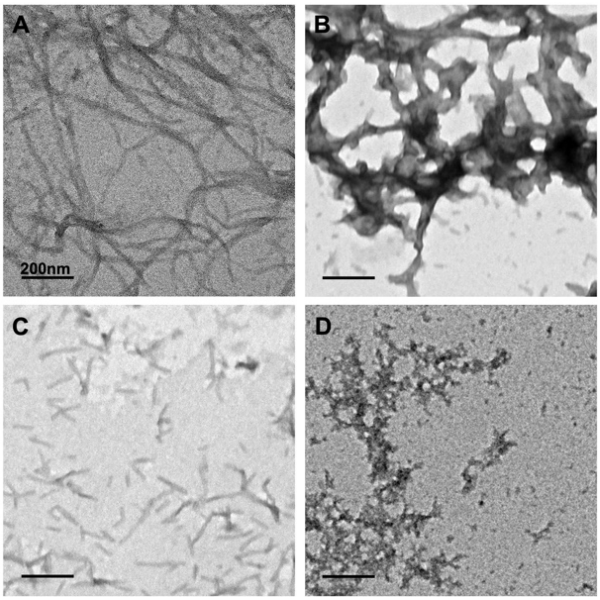


**Figure S1. TEM iamges of KD-n at pH 7.4.** (A) KD-1; (B) KD-2; (C) KD-3; (D) KD-4.

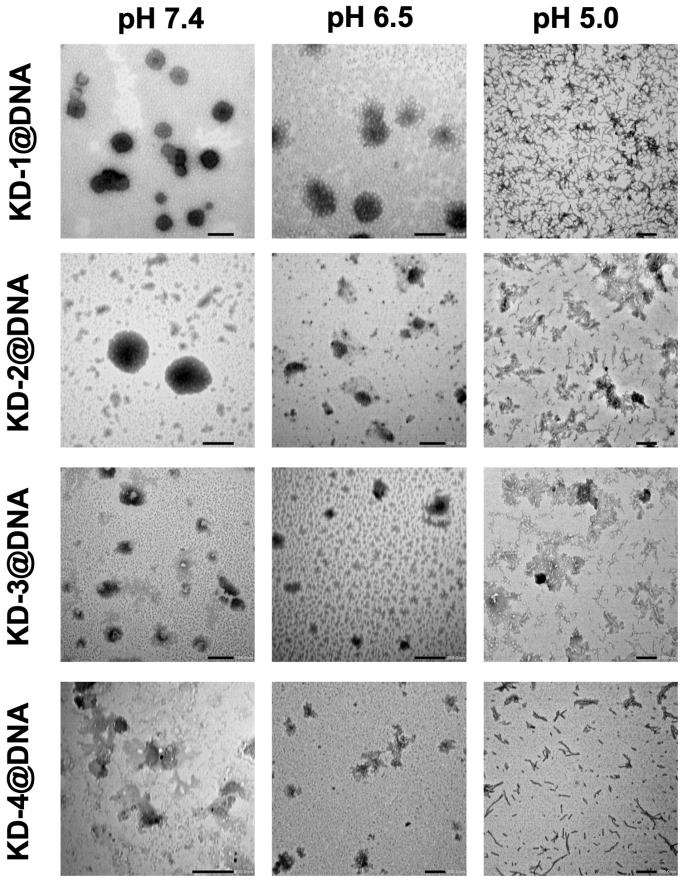


**Figure S2. TEM images of KD-n@ DNA incubated in pH 7.4, pH 6.5, and pH 5.0 buffer solutions for 4 h**.

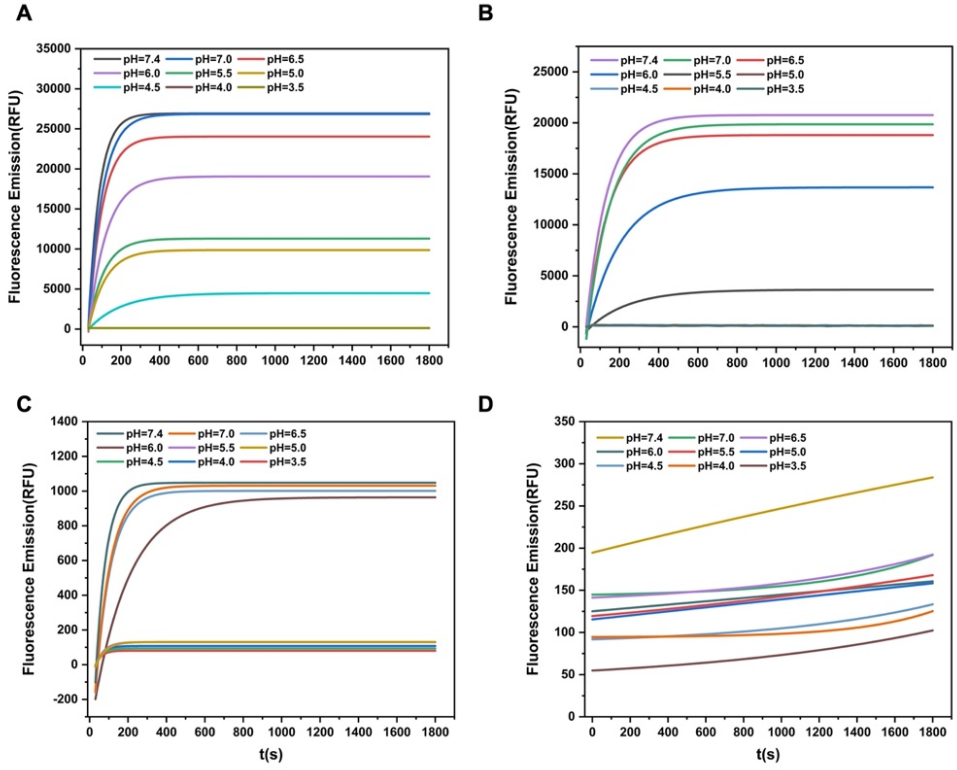


**Figure S3. The fluorescence intensity curve of ANS as a fluorescent probe assembled with KD-n at different pH.** (A) KD-1; (B) KD-2; (C) KD-3; (D) KD-4.

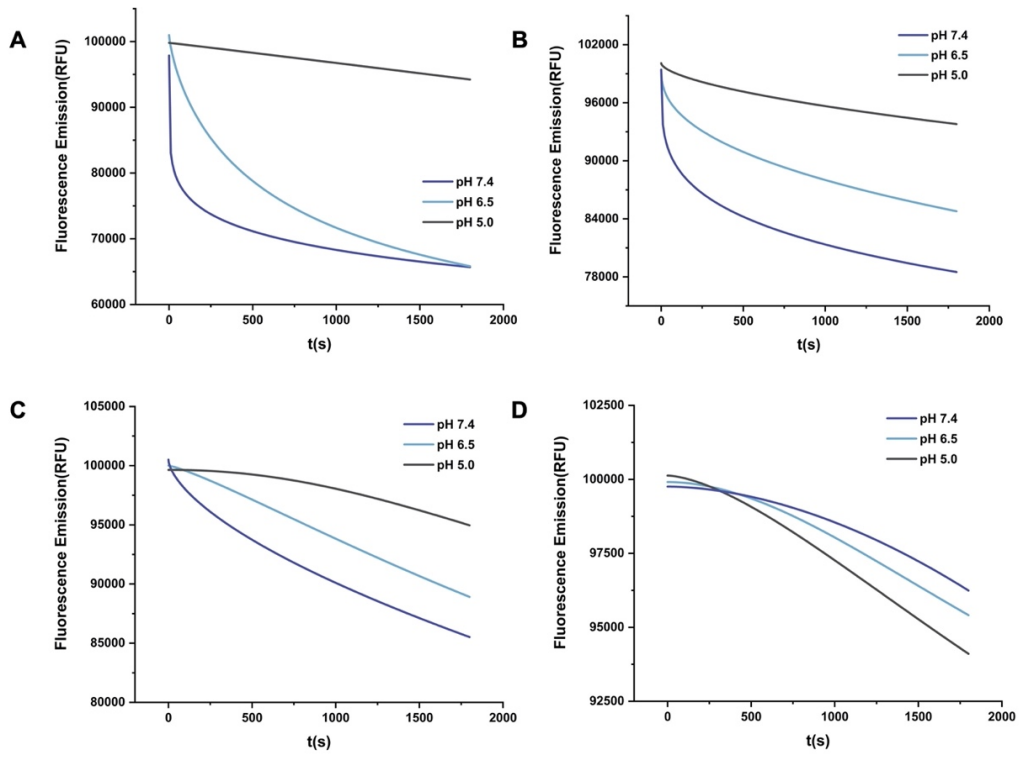


**Figure S4. Kinetic measurements.** (A) KD-1; (B) KD-2; (C) KD-3; (D) KD-4

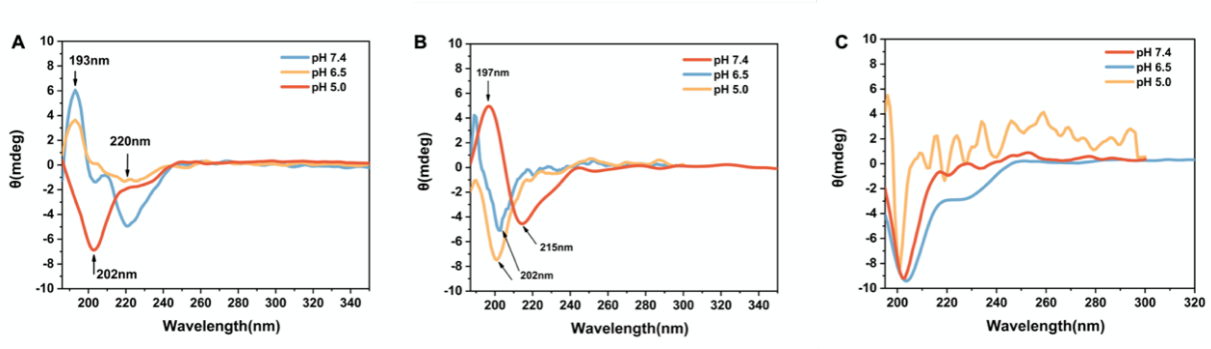


**Figure S5. Circular Dichroism Spectroscopy of KD-n@DNA at pH 7.4, pH 6.5 and pH 5.0.** (A)KD-2; (B)KD-3; (C)KD-4

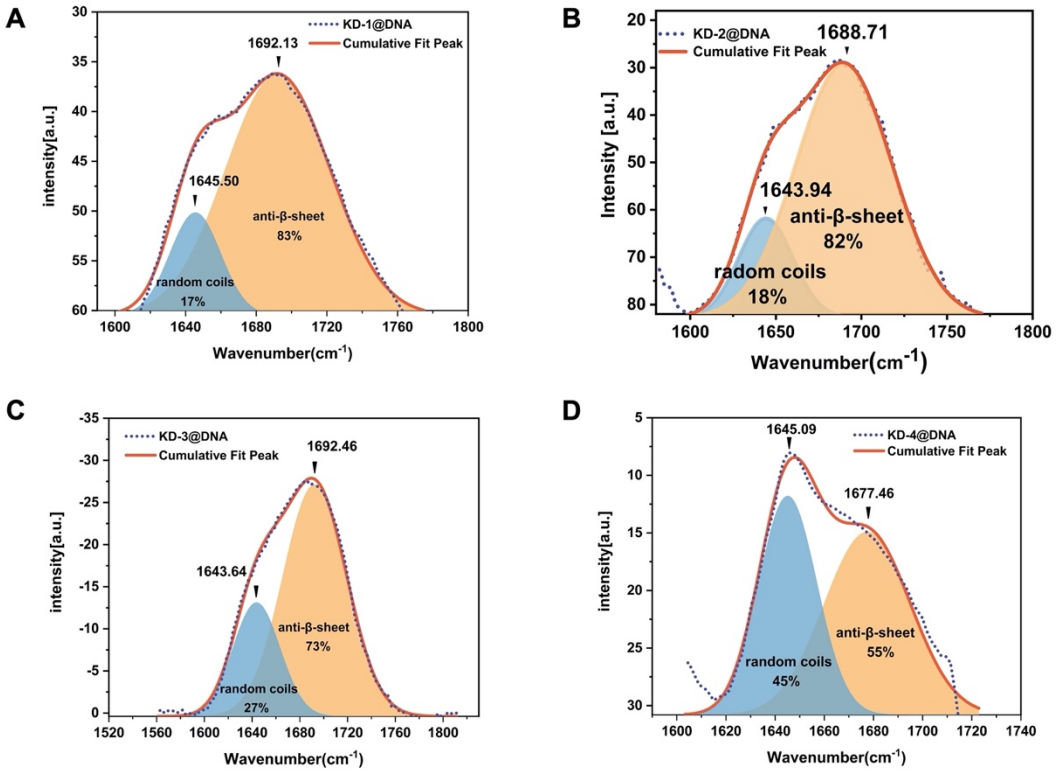


**Figure S6. Fourier Transform Infrared Spectroscopy of KD-n at pH 7.4, pH 6.5 and pH 5.0.** (A) KD-1; (B) KD-2; (C) KD-3;(D) KD-4

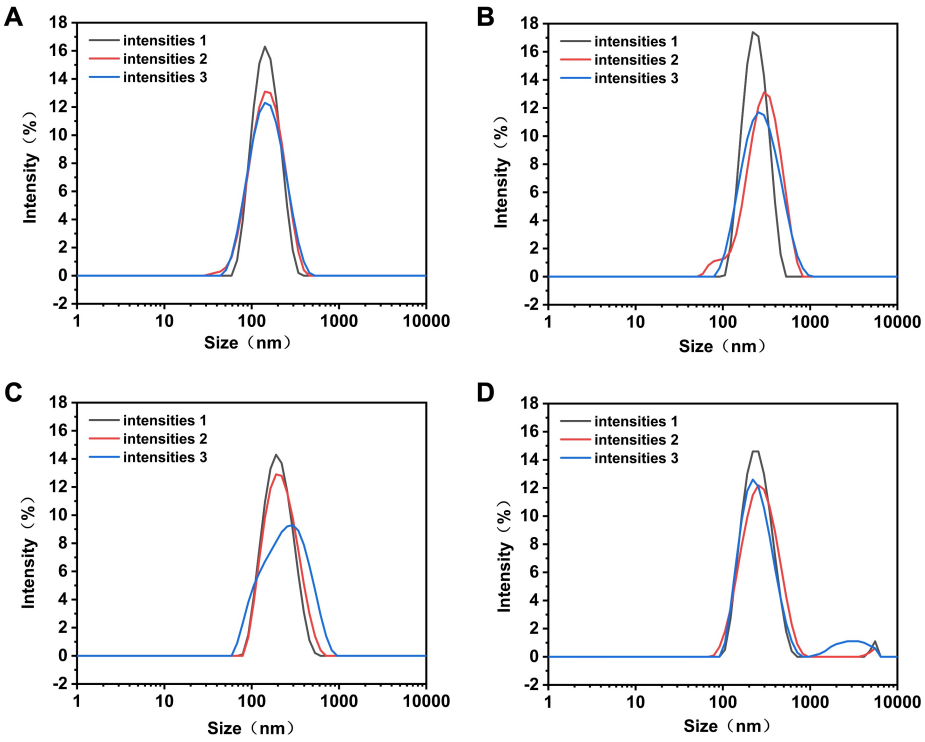


**Figure S7. Particle size distribution plot of KD-n@DNA at pH 7.4.** (A) KD-1; (B) KD-2; (C) KD-3; (D) KD-4

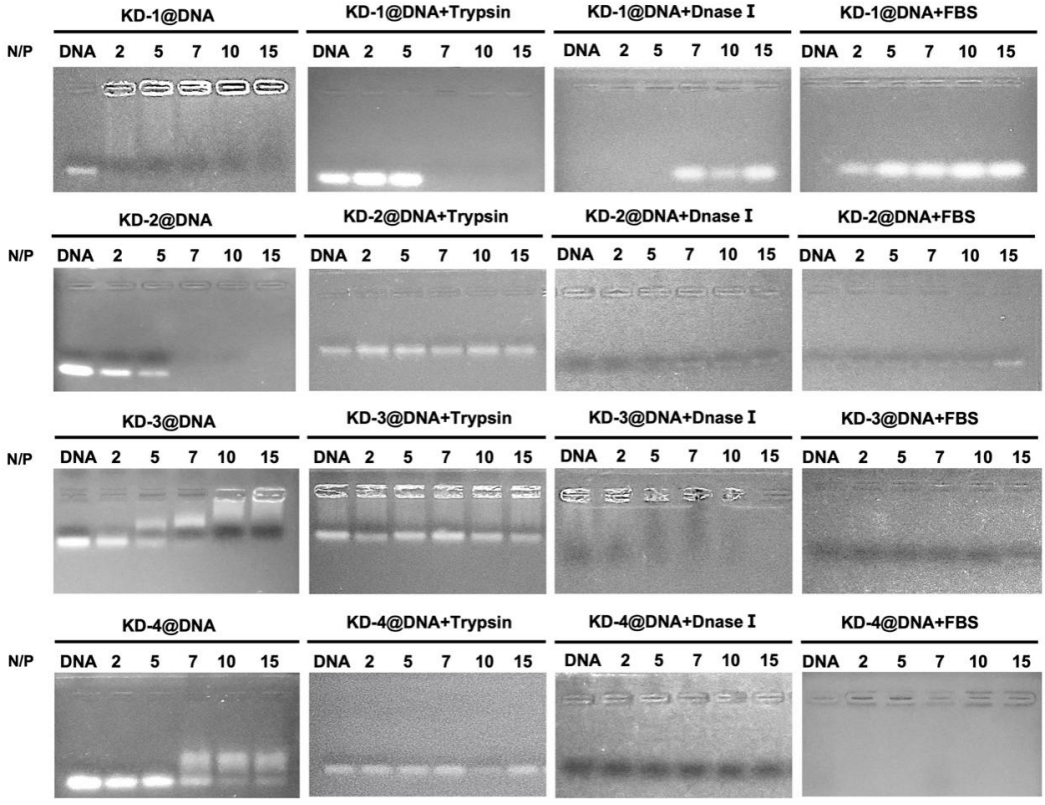


**Figure S8. EMSAs of KD-n@DNA treated with Trypsin, Dnase I, and fetal bovine serum (FBS).**

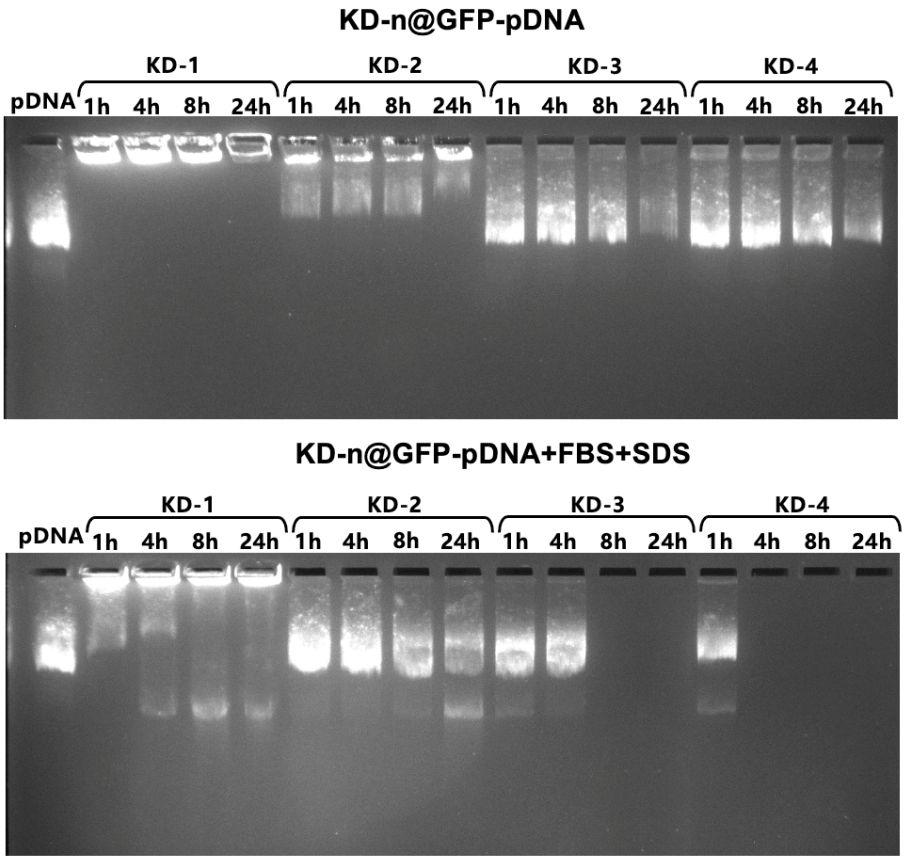


**Figure S9. Serum stability of KD-n@GFP-pDNA nanoparticles for 24 h at 37°C.**

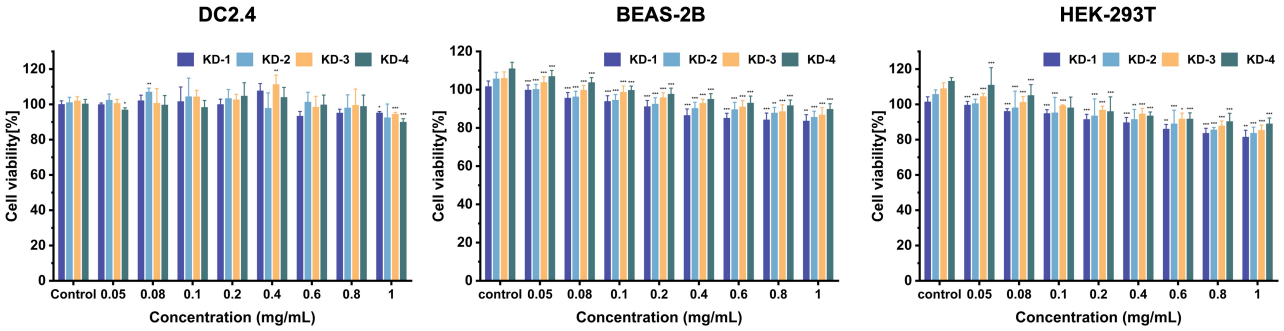


**Figure S10. In vitro cytotoxicity of KD-n and control against DC2.4 cells, BEAS-2B cells and HEK-293T cells after 48 h of incubation. **, $p<0.01$; ***, $p<0.001$.**

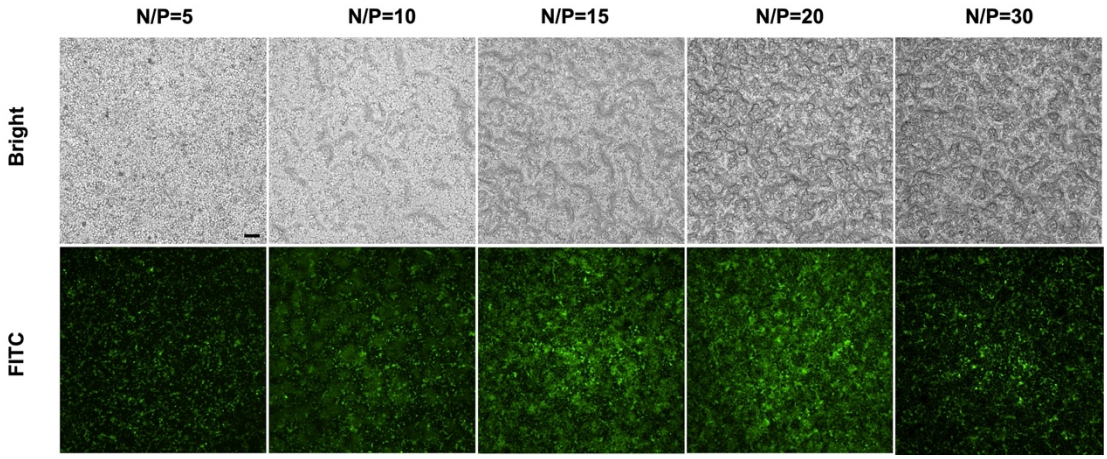


**Figure S11. Fluorescent microscopy analysis of Hela cells treated with KD-1@FAM-siRNA for 4 h. Scale bar:400 μm.**

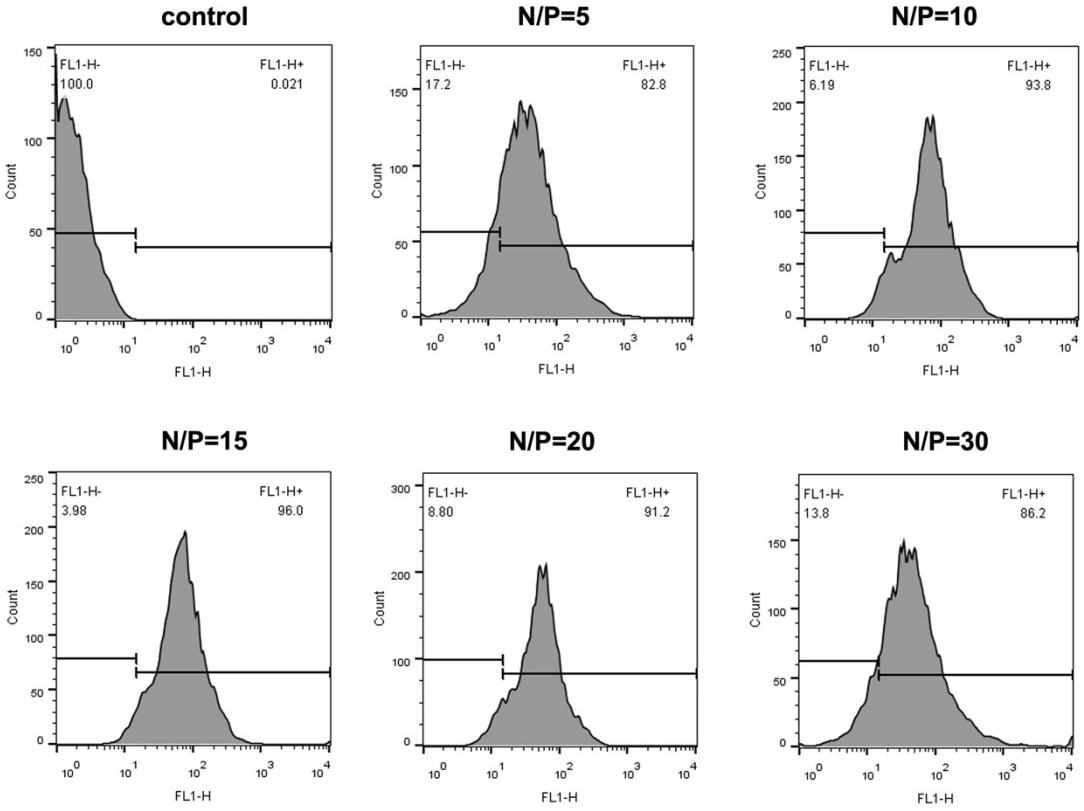


**Figure S12. Flow cytometric analyses of Hela cells treated with KD-1@FAM-siRNA for 4 h.**

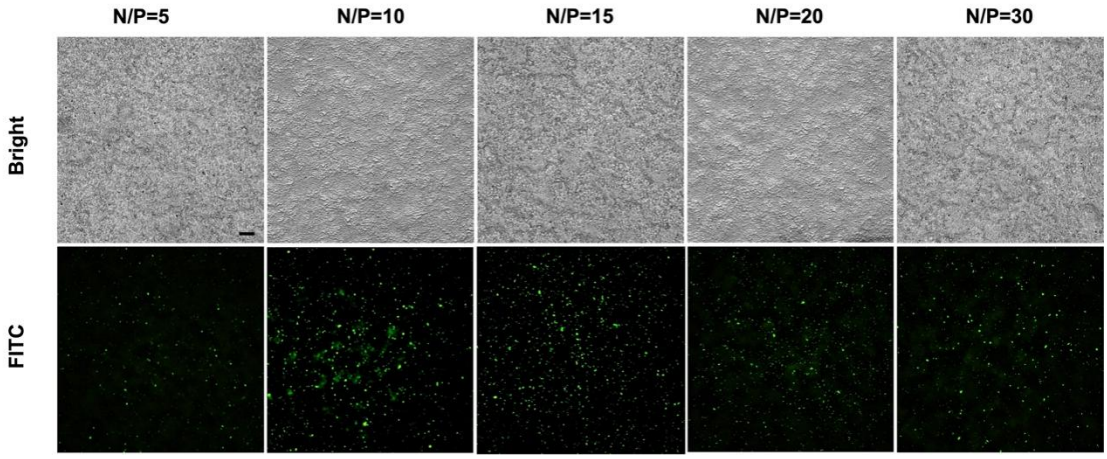


**Figure S13. Fluorescent microscopy analysis of Hela cells treated with KD-2@FAM-siRNA for 4 h. Scale bar:400 μm.**

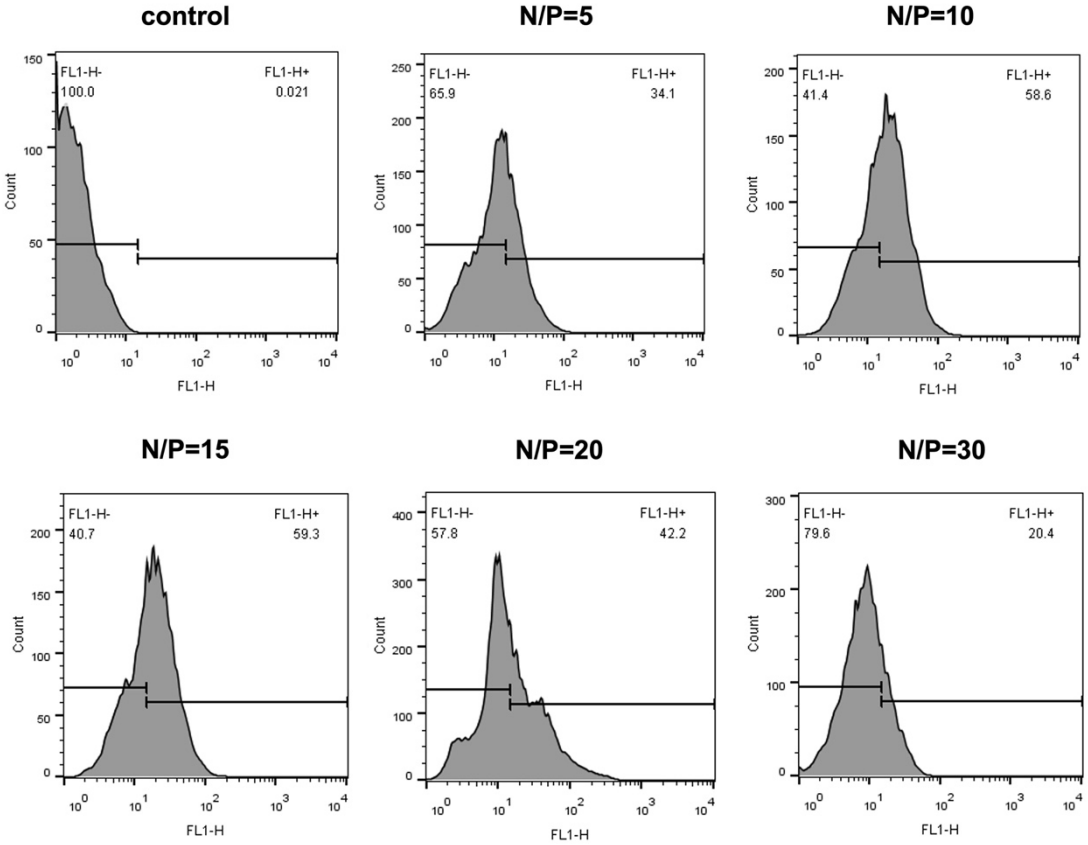


**Figure S14. Flow cytometric analyses of Hela cells treated with KD-2@FAM-siRNA for 4 h.**

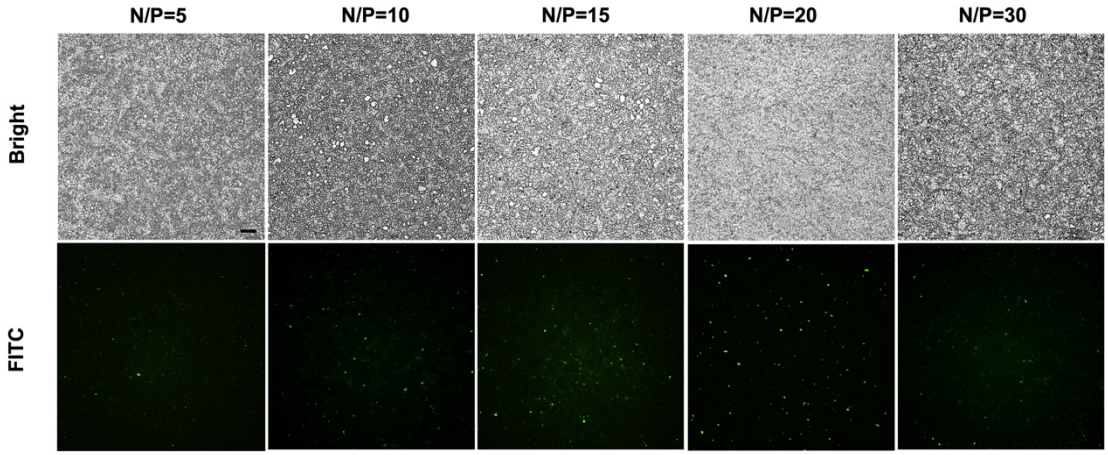


**Figure S15. Fluorescent microscopy analysis of Hela cells treated with KD-3@FAM-siRNA for 4 h. Scale bar:400 μm.**

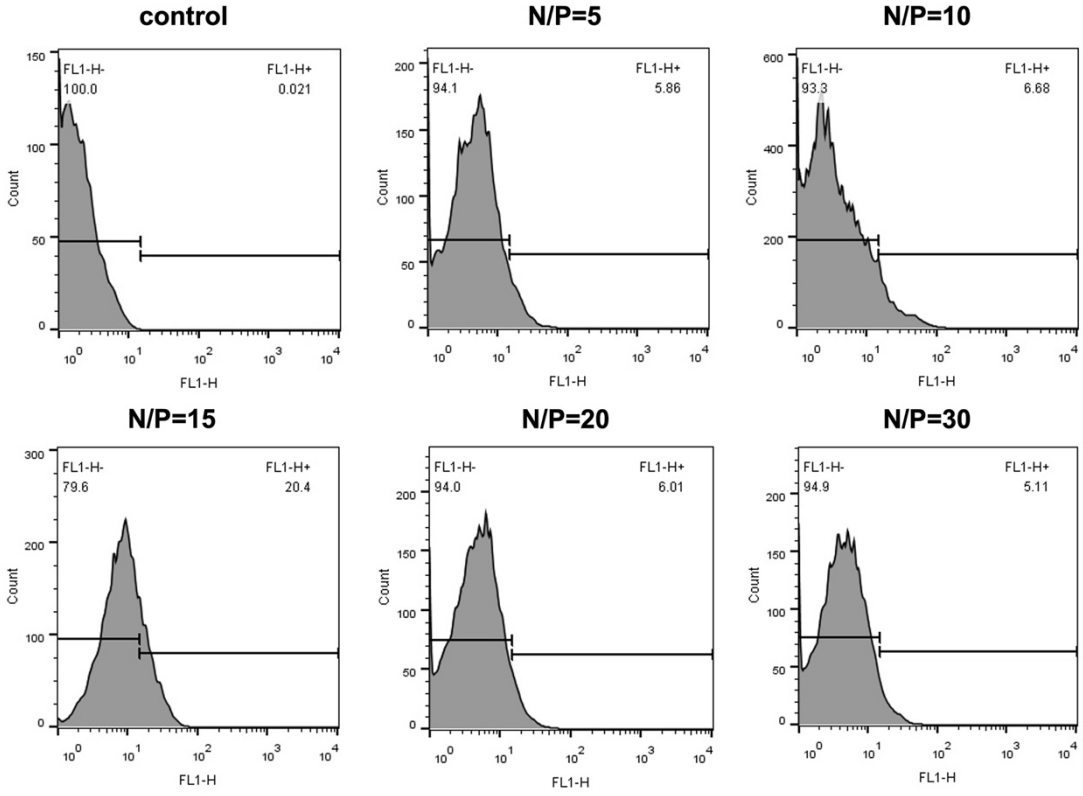


**Figure S16. Flow cytometric analyses of Hela cells treated with KD-3@FAM-siRNA for 4 h.**

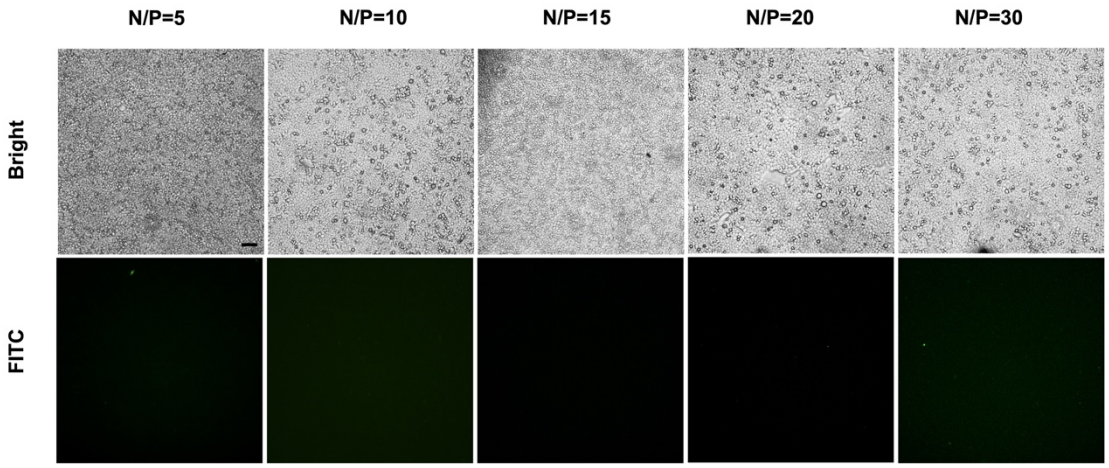


**Figure S17. Fluorescent microscopy analysis of Hela cells treated with KD-4@FAM-siRNA for 4 h. Scale bar:400 μm.**

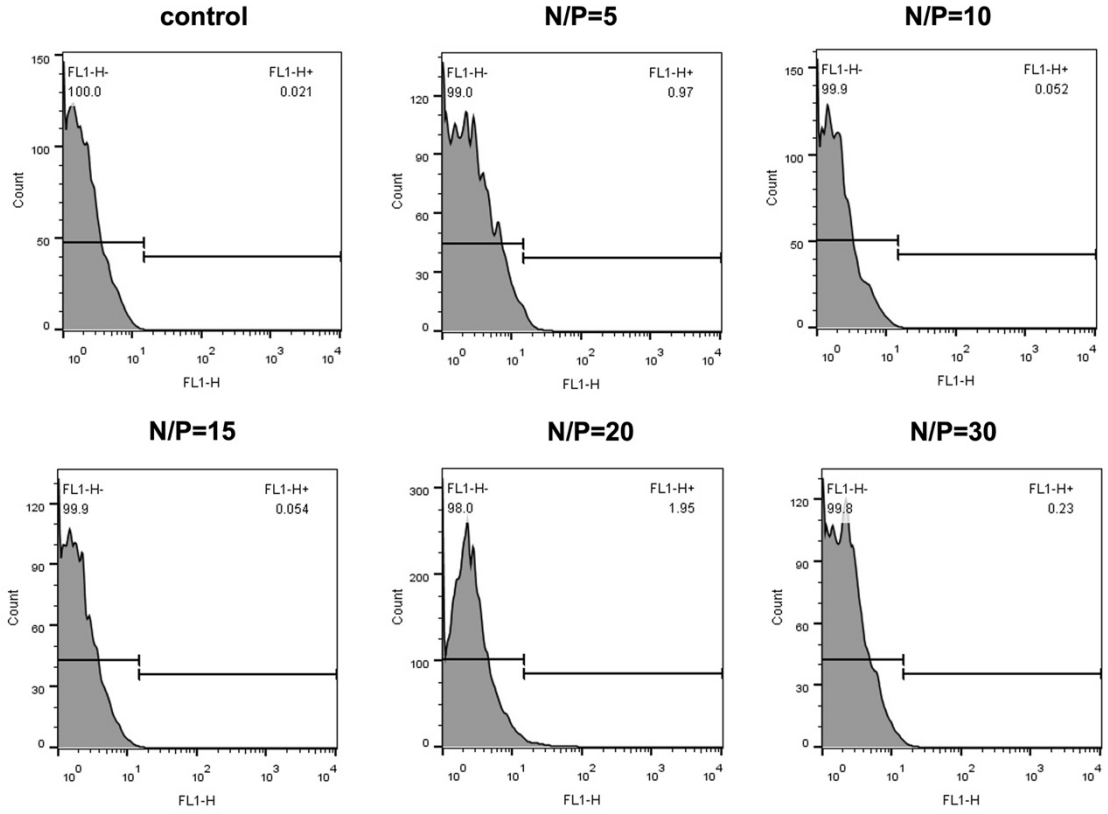


**Figure S18. Flow cytometric analyses of Hela cells treated with KD-4@FAM-siRNA for 4 h.**

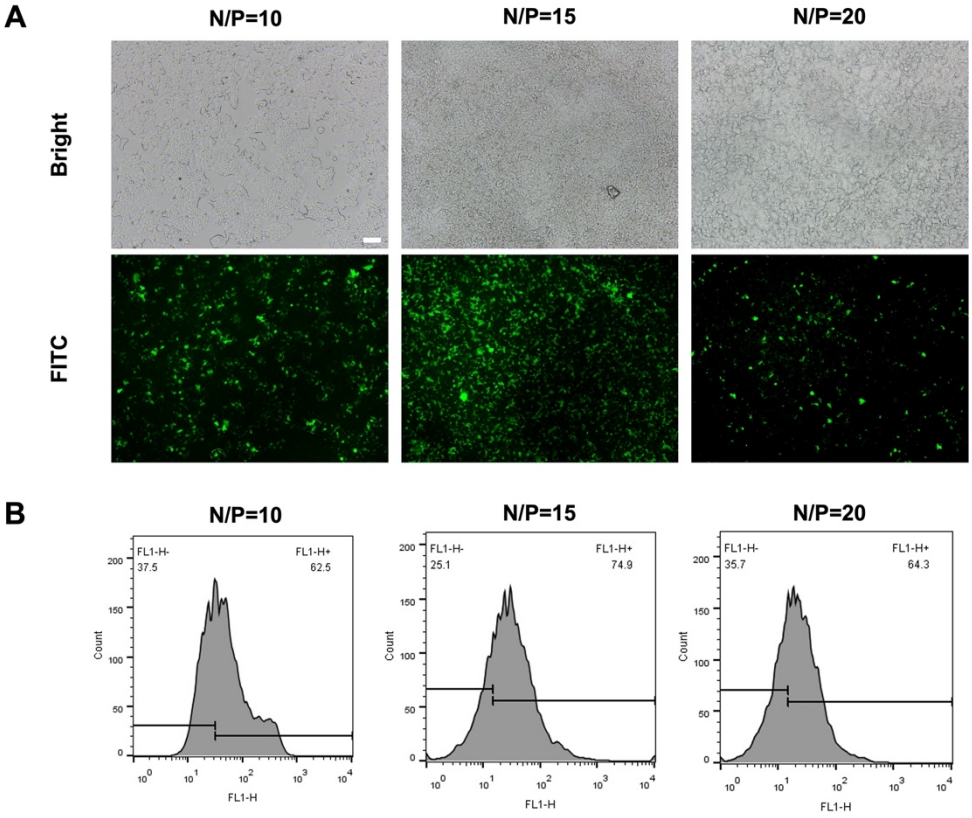


**Figure S19. (A)Fluorescent microscopy analysis and (B) flow cytometric analysis of Hela cells treated with KD-1@GFP-mRNA for 48 h. Scale bar:200 μm.**

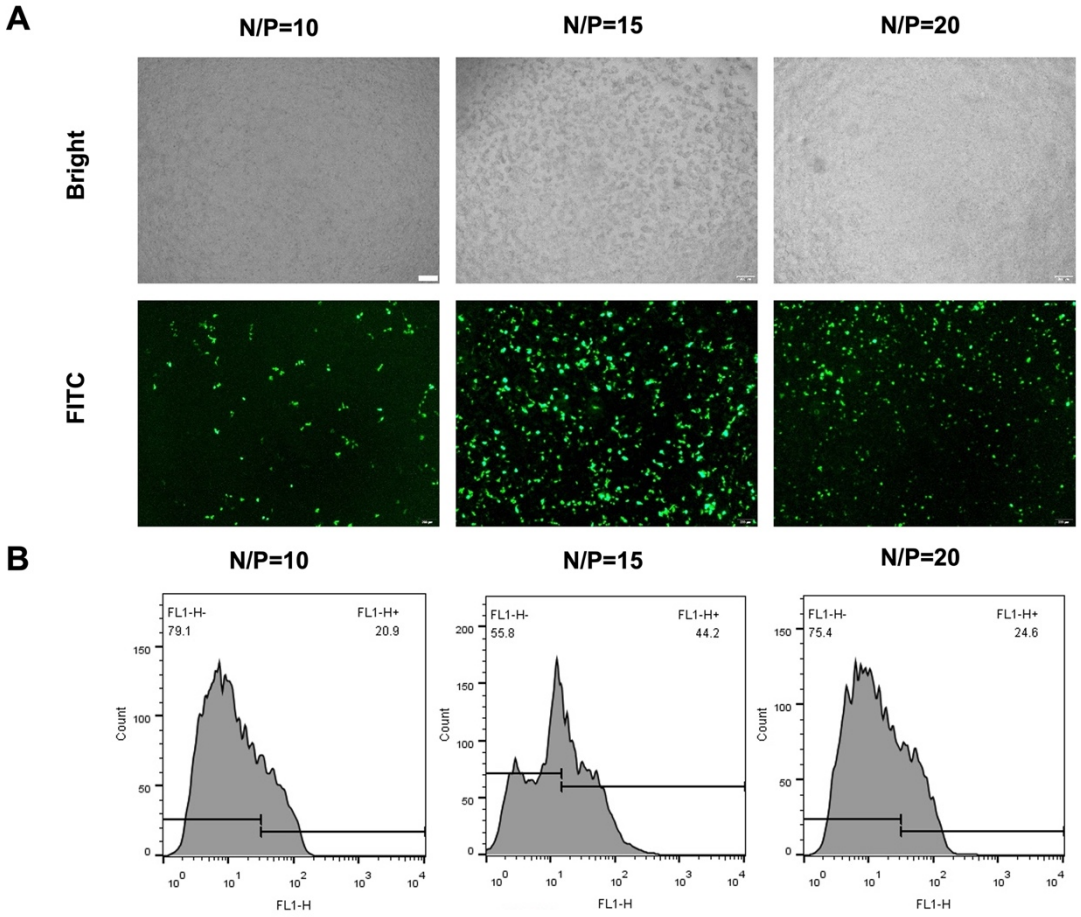


**Figure S20. (A)Fluorescent microscopy analysis and (B) flow cytometric analysis of Hela cells treated with KD-2@GFP-mRNA for 48 h. Scale bar:200 μm.**

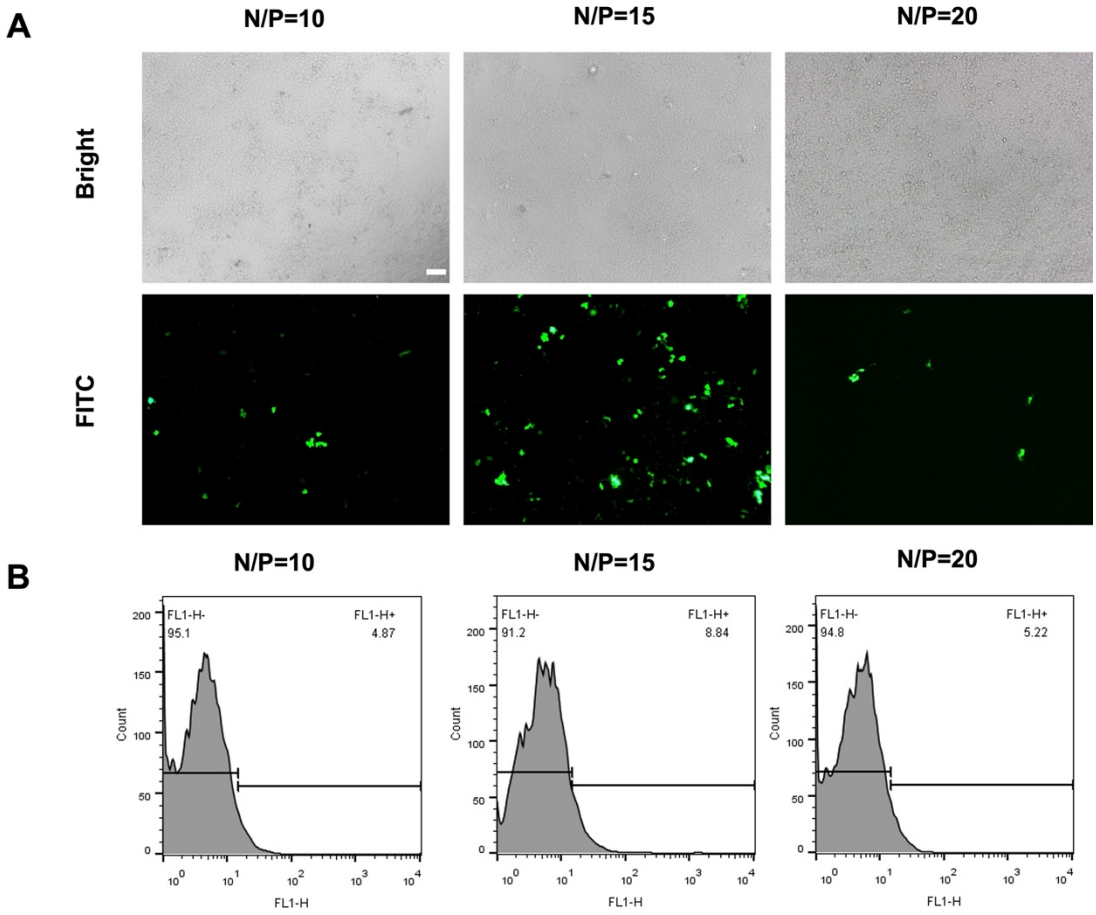


**Figure S21. (A)Fluorescent microscopy analysis and (B) flow cytometric analysis of Hela cells treated with KD-3@GFP-mRNA for 48 h. Scale bar:200 μm.**

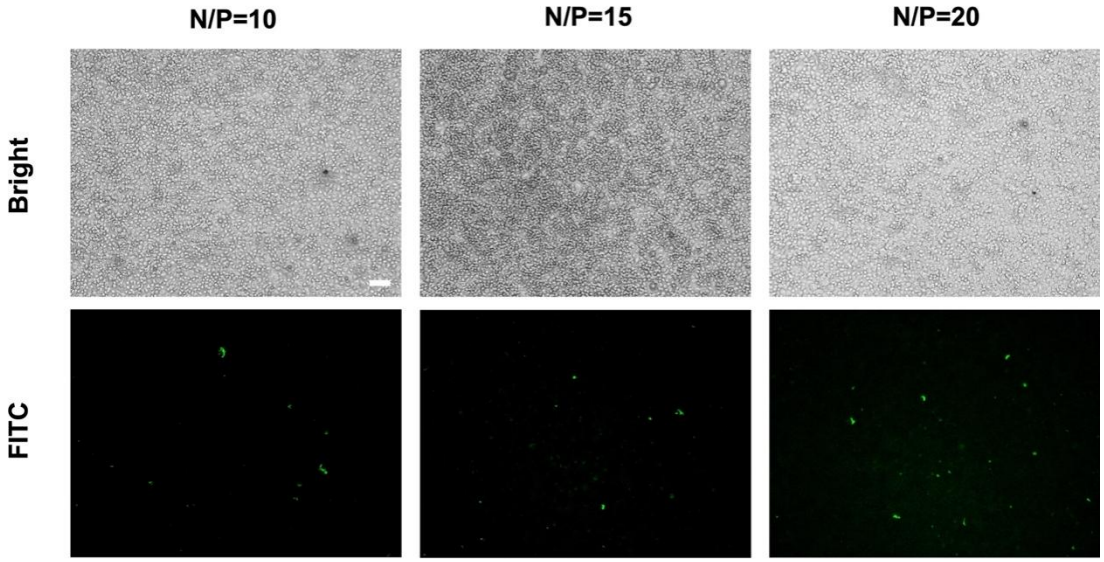


**Figure S22. Fluorescent microscopy analysis of Hela cells treated with KD-4@GFP-mRNA for 48 h. Scale bar:200 μm.**

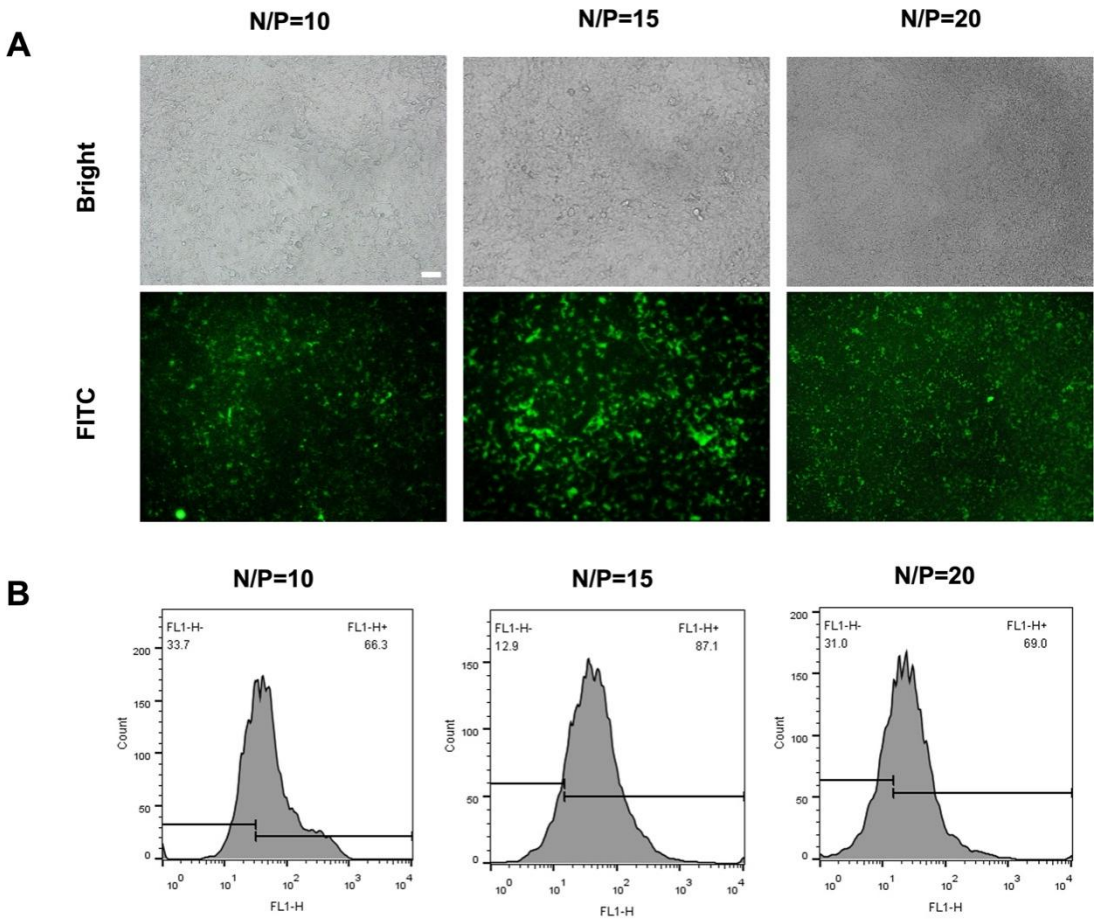


**Figure S23. (A)Fluorescent microscopy analysis and (B) flow cytometric analysis of Hela cells treated with KD-1@GFP-pDNA for 48 h. Scale bar:200 μm.**

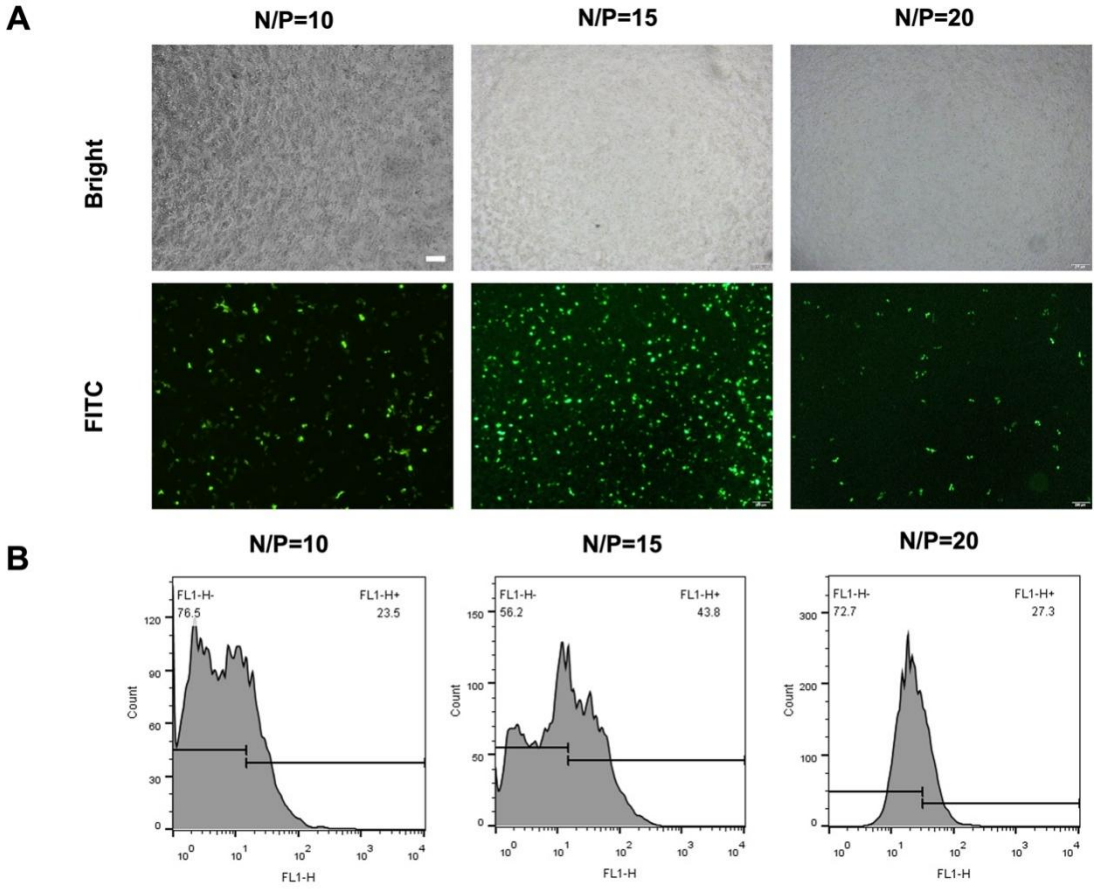


**Figure S24. (A)Fluorescent microscopy analysis and (B) flow cytometric analysis of Hela cells treated with KD-2@GFP-pDNA for 48 h. Scale bar:200 μm.**

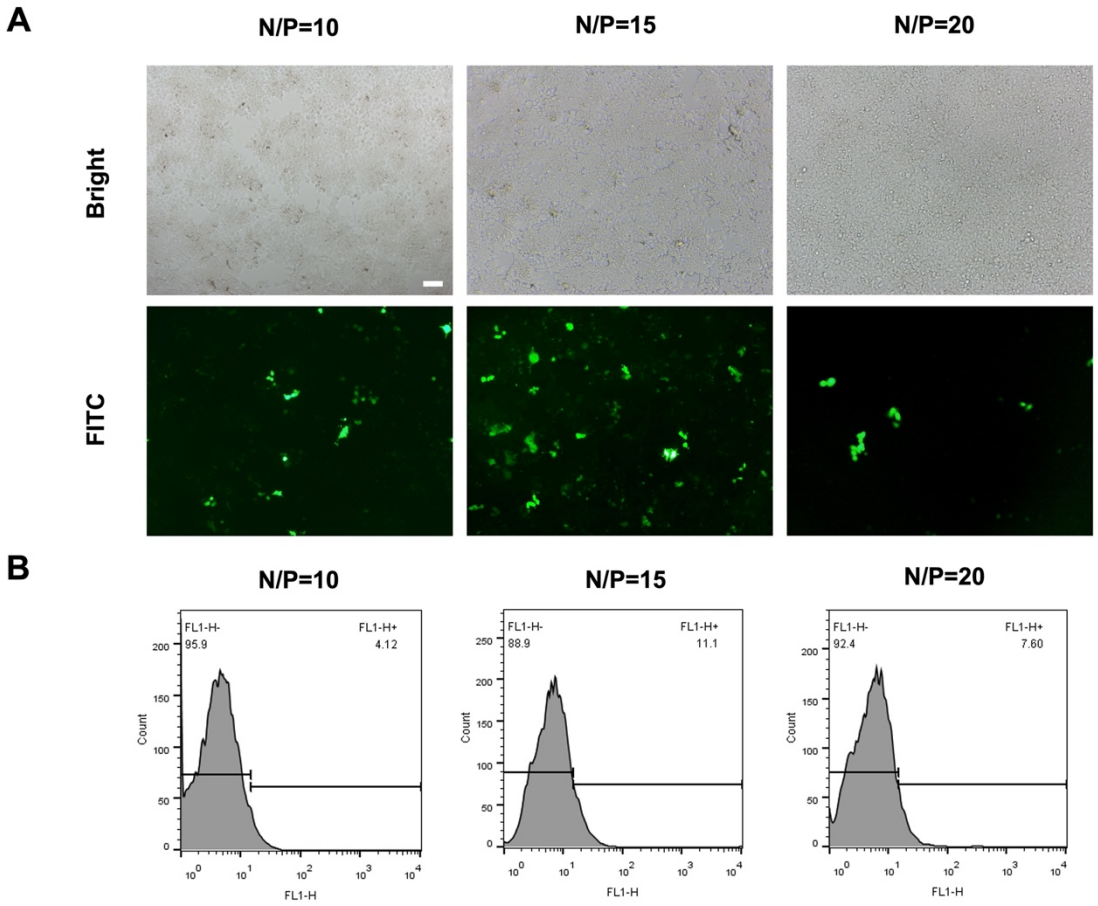


**Figure S25. (A)Fluorescent microscopy analysis and (B) flow cytometric analysis of Hela cells treated with KD-3@GFP-pDNA for 48 h. Scale bar:200 μm.**

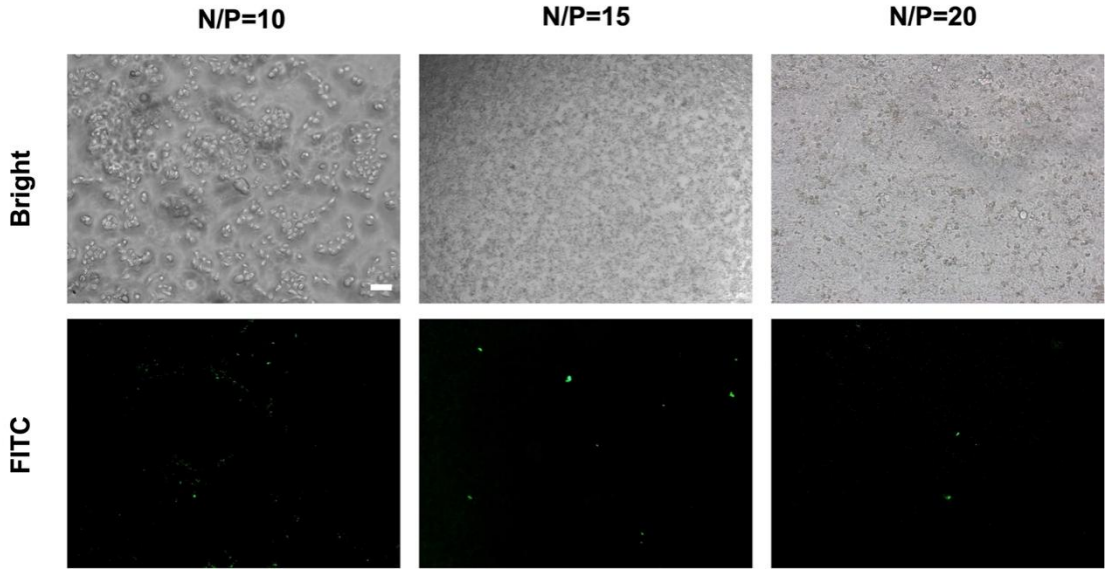


**Figure S26. Fluorescent microscopy analysis of Hela cells treated with KD-4@GFP-pDNA for 48 h. Scale bar:200 μm.**

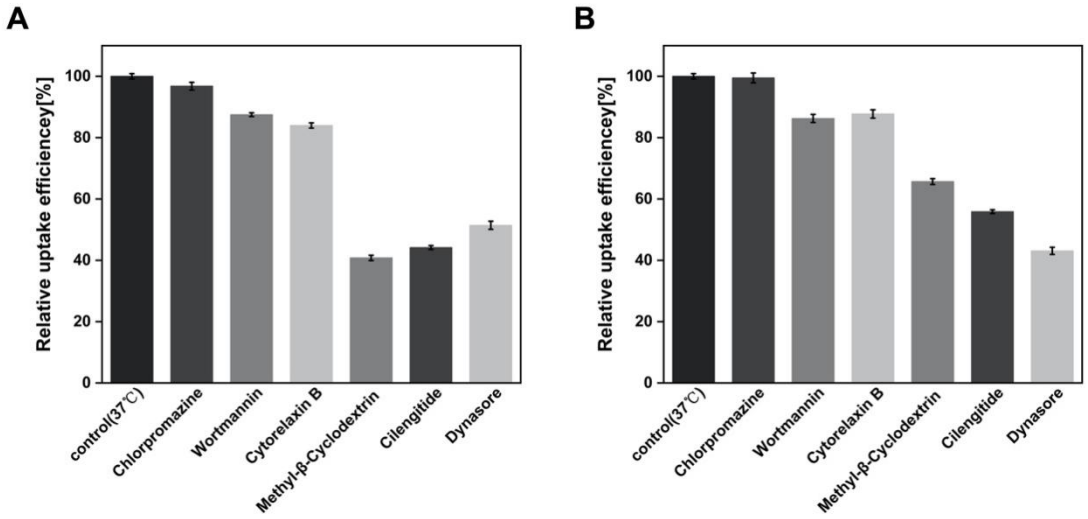


**Figure S27. Uptake efficiency of Hela cells treated with FITC-labeled KD-n@siRNA in the presence of inhibitors. (A) KD-2; (B) KD-3**

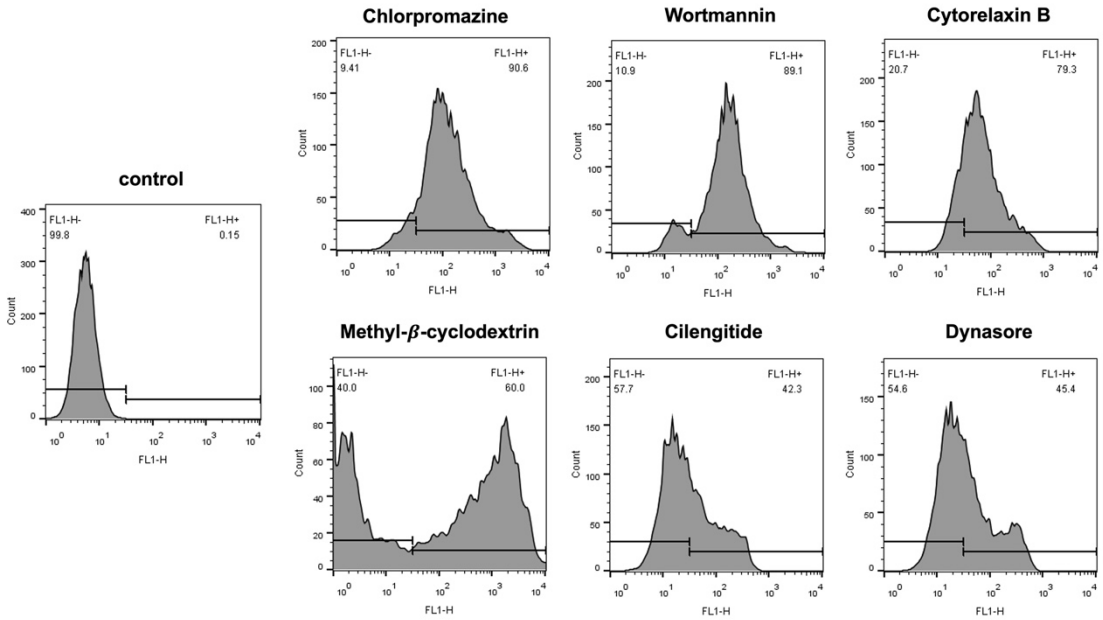


**Figure S28. Flow cytometric analysis of Hela cells treated with FITC-labeled KD-1@siRNA in the presence of inhibitors.**

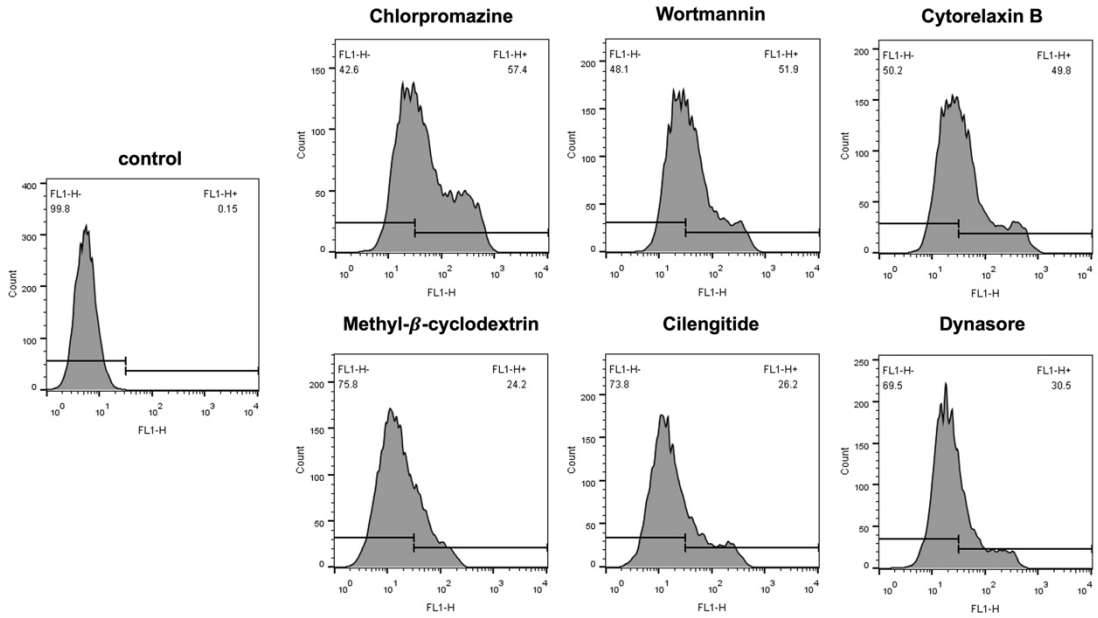


**Figure S29. Flow cytometric analysis of Hela cells treated with FITC-labeled KD-2@siRNA in the presence of inhibitors.**

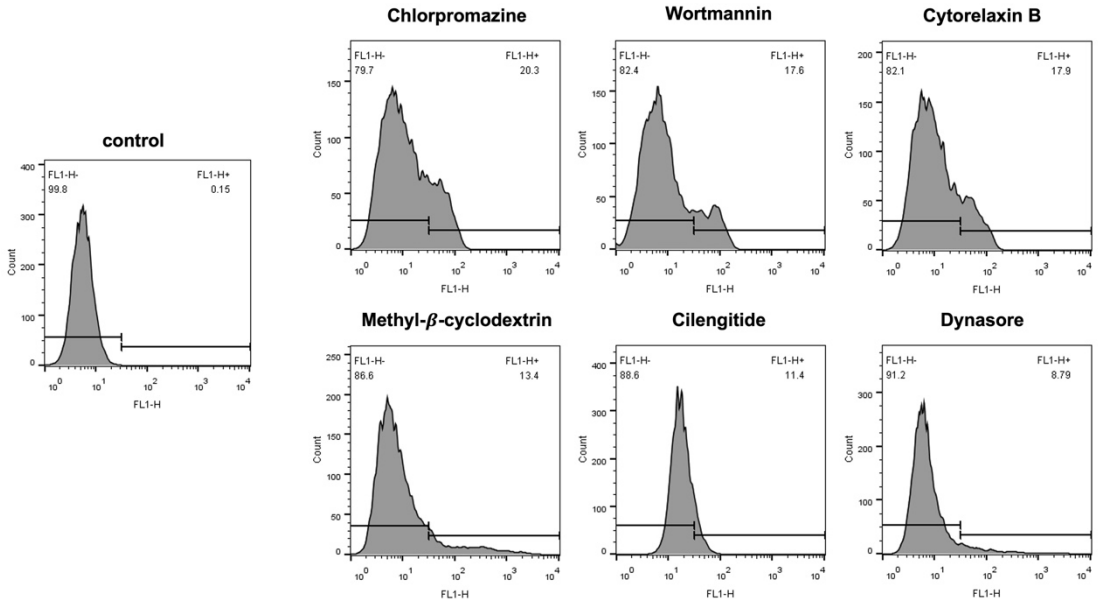


**Figure S30. Flow cytometric analysis of Hela cells treated with FITC-labeled KD-3@siRNA in the presence of inhibitors.**

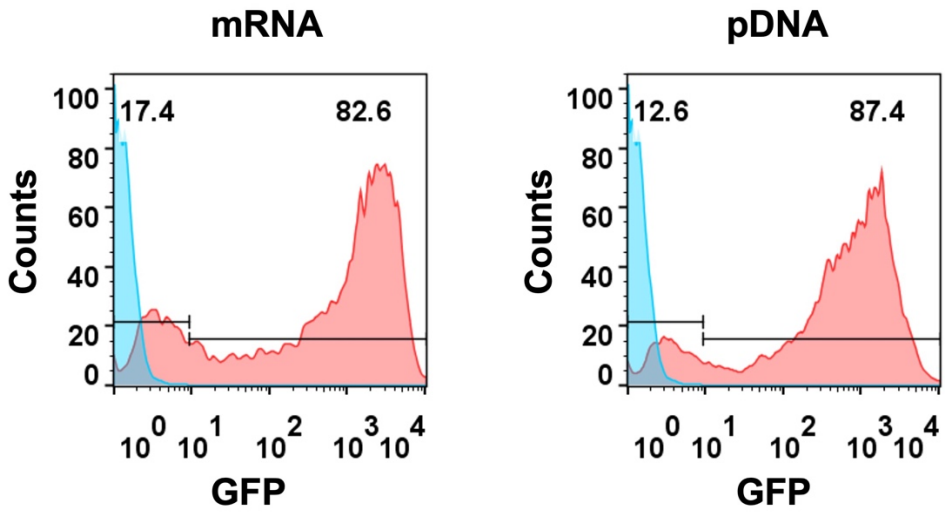


**Figure S31. Flow cytometric analysis of Hela cells treated with *Lipofectamine 2000* for 48 h.**

## S-II peptide sequences

**Table S1** Peptides reported in this study

| Name | Sequence | Molecular weight (Da) | $pH_0$ |
|---|---|---|---|
| KD-1 | KKKHHHH-Acp-LLLLLLLLGSPDRGD | 2654.16 | 5.5 |
| KD-2 | KKK-Acp-LLHLLHLLHGSPDRGD | 2290.71 | 5.8 |
| KD-3 | KKKHHHH-Acp-LLLLGSPDRGD | 2201.53 | 6.0 |
| KD-4 | KKKHHHH-Acp-GSPDRGD | 1748.90 | none |

Acp stands for 6-Aminocaproic acid. The amino acids in the peptide are L-type amino acids.