Supplementary Information

Forecasting the Reaction of DNA Modifying Enzymes on DNA Nanostructures by Coarse Grained Model for Stimuli-Responsive Drug Delivery

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Content

Supporting Figures

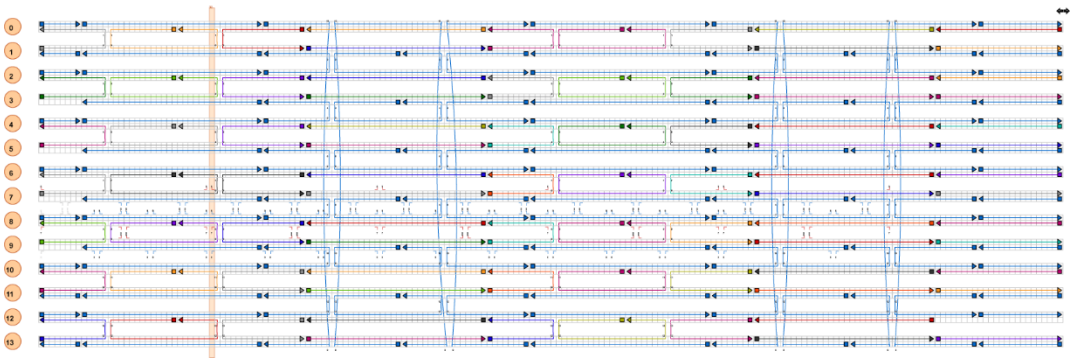

Figure S1. The design of DNA nanotubes using by caDNAno as the input of simulation platform oxDNA. The circumference of each nanotubes is 7 tiles and the length is 4 tiles.

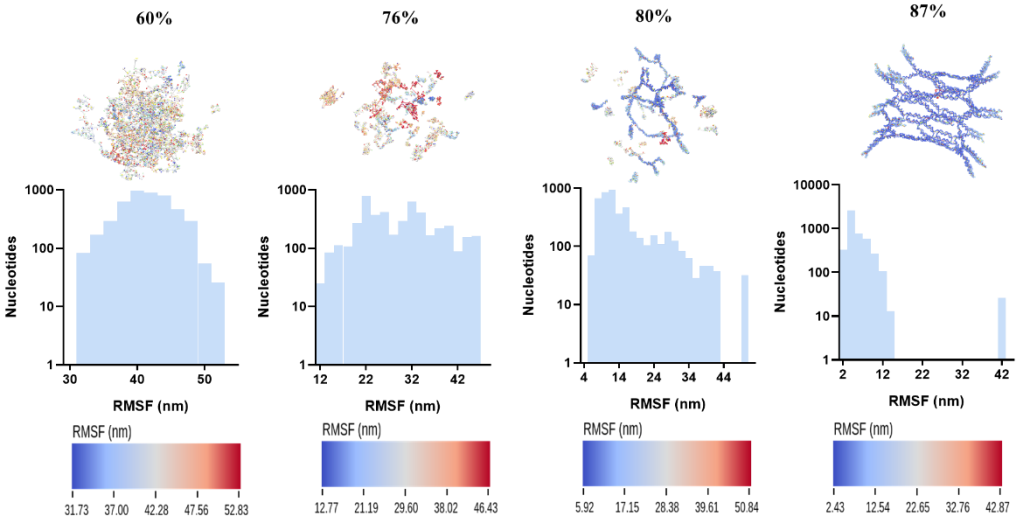

Figure S2. The simulation confirmation of DNA nanotube (no uracil) under different hydrogen bond strength. Monovalent cation concentration is 0.09397 M.

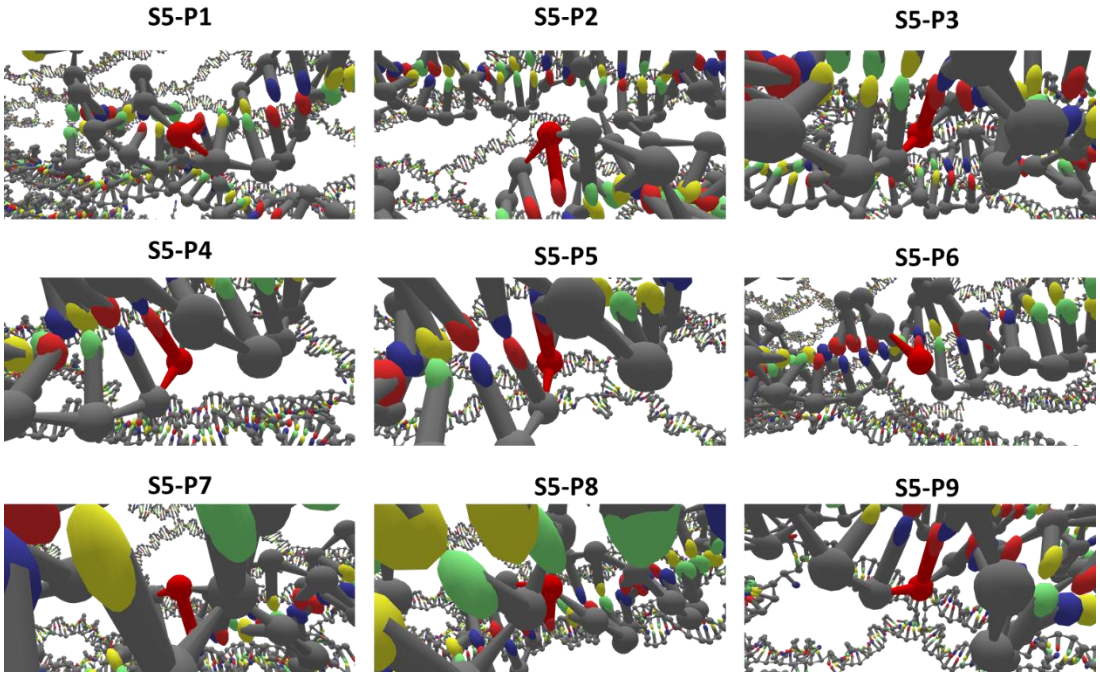

Figure S3. Base orientation of the nine candidate positions on the S5 strand (presented by oxView).

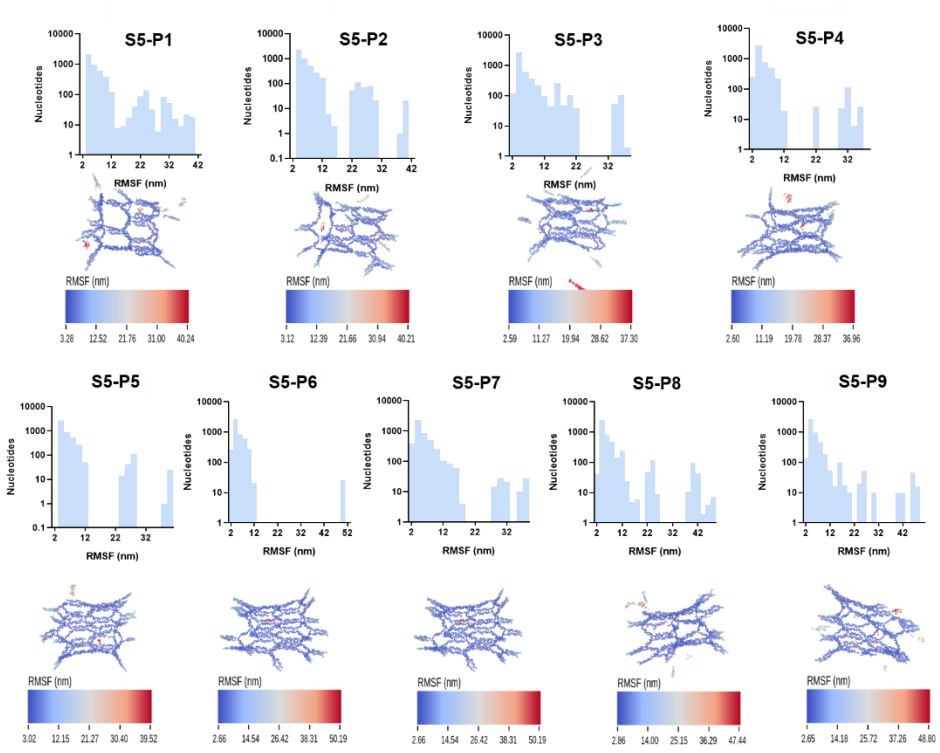

Figure S4. The mean structure and RMSF distribution of the 9 kinds of DNA nanotubes with one-base gap on the S5 strand.

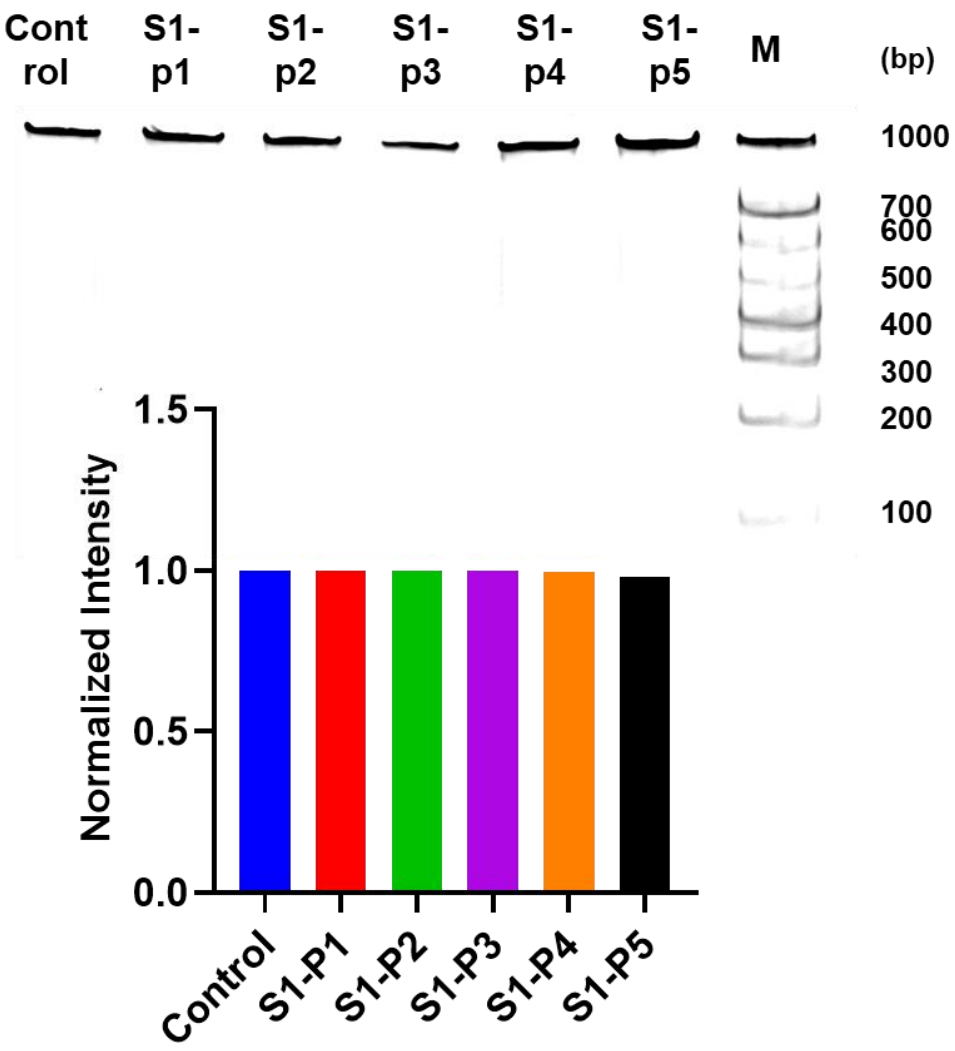

Figure S5. Characterization of DNA nanotubes by gel electrophoresis. Control is the non-uracil nanotube; the others are uracil-containing nanotubes. The band intensity is normalized to project.

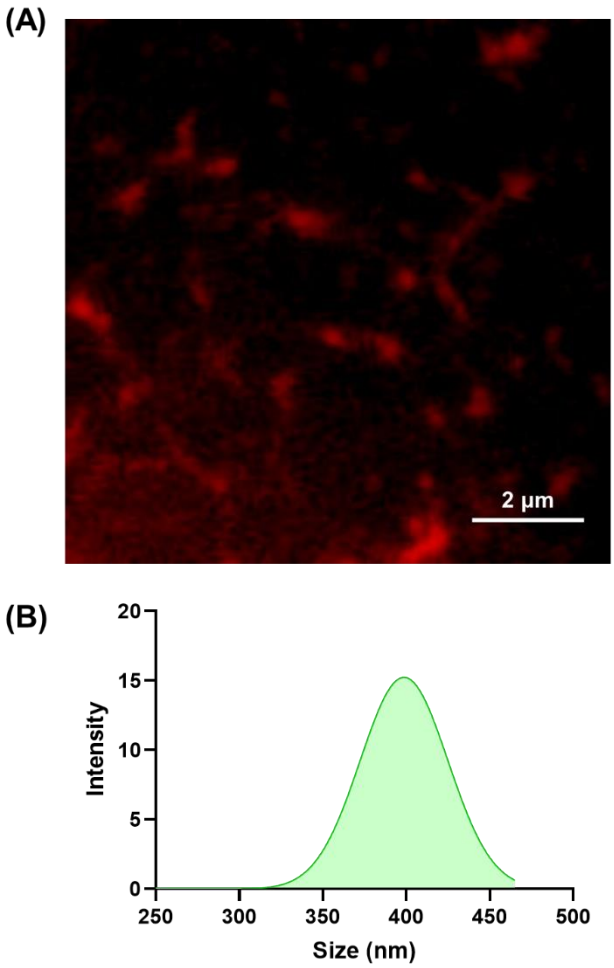

Figure S6. (A) TIRF image of the non-uracil DNA nanotube. The S3 strand was Cy5 labeled. (B) DLS measurement of the DNA nanotube.

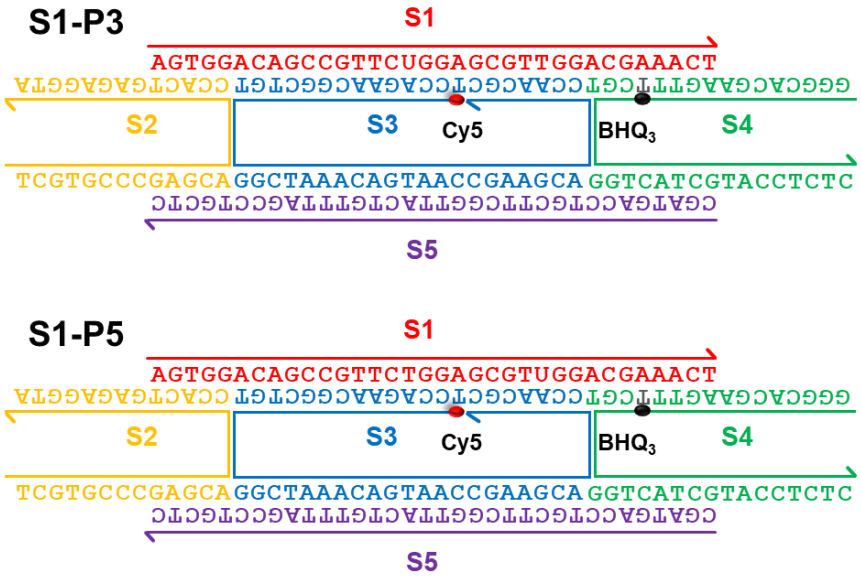

Figure S7. Scheme of fluorophore and quencher labeled DNA tiles.

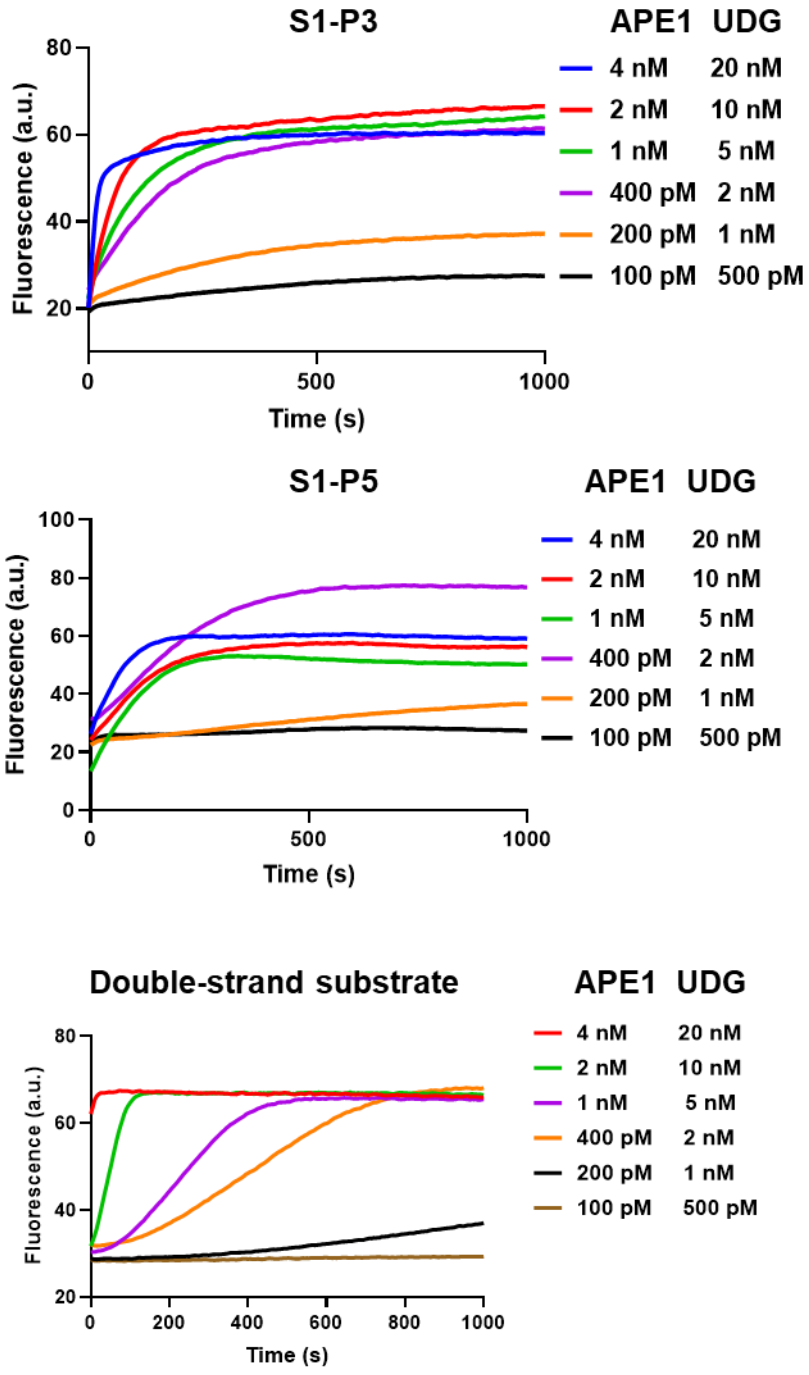

Figure S8. The sensitivity of DNA nanotubes and double-stranded substrate towards UDG and APE1.

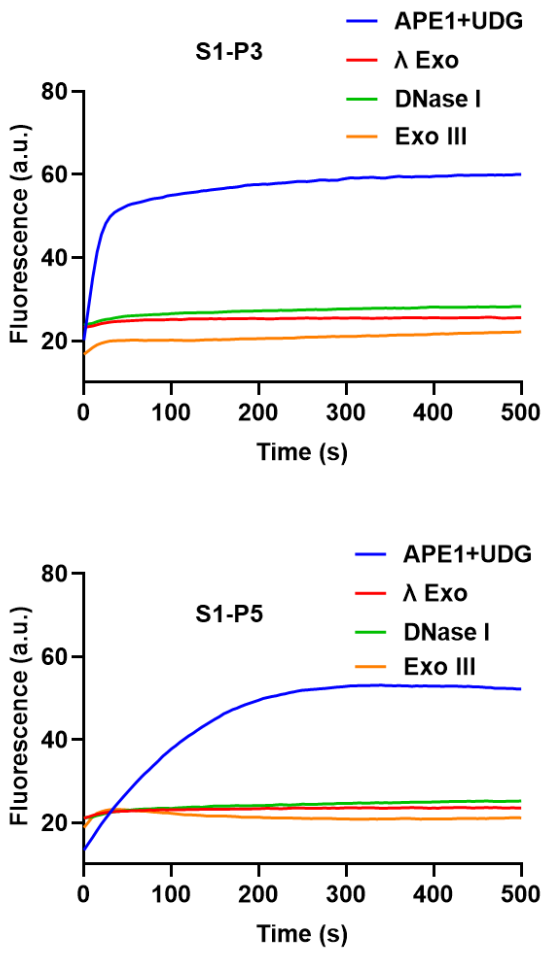

Figure S9. The reactivity of uracil-containing nanotubes for different DNA modifying enzymes. UDG was 20nM and the other enzymes was 4 nM.

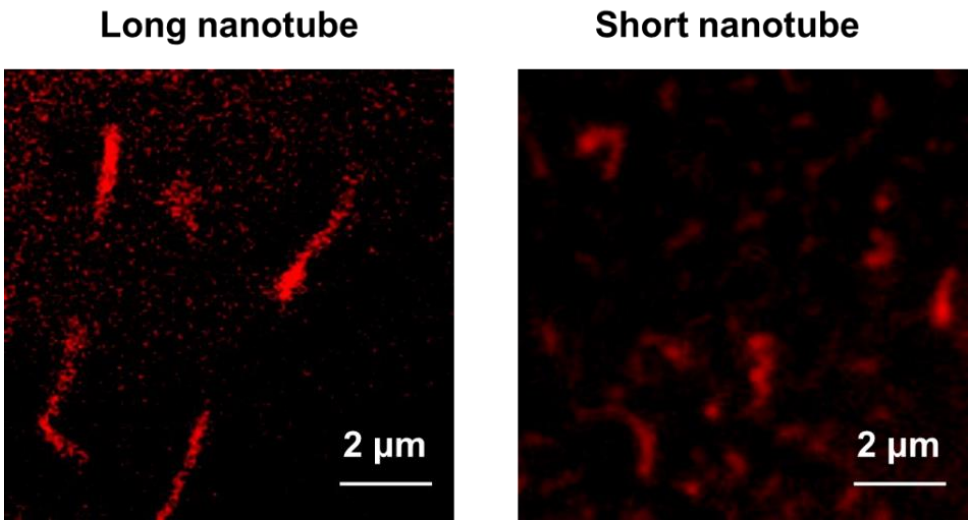

Figure S10. TIRF images of DNA nanotubes with different length. Long and short nanotubes were assembled by 18h and 1.5h strand annealing, respectively.

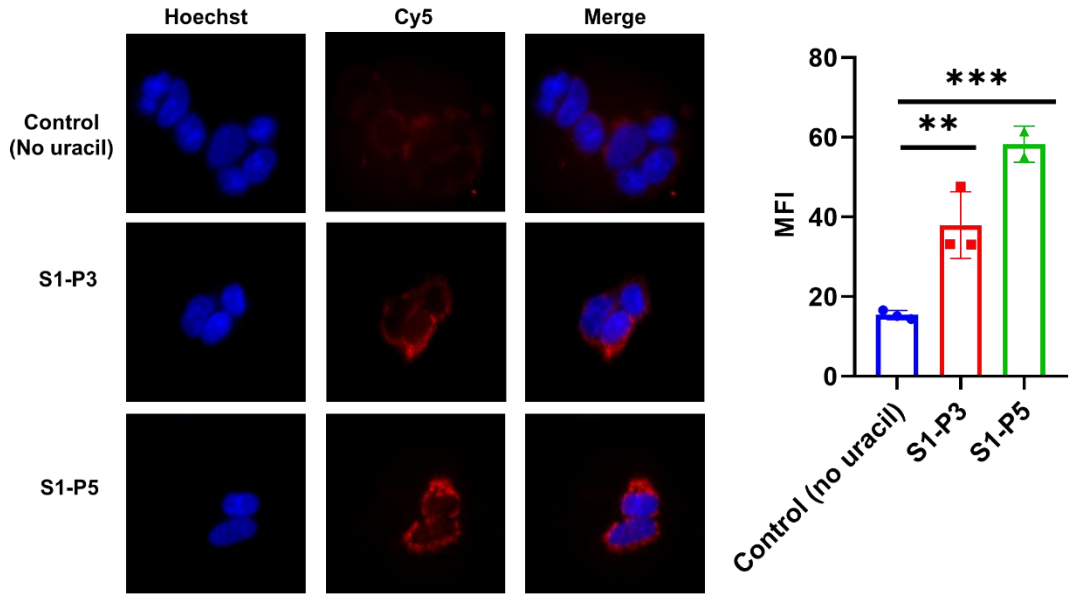

Figure S11. HILO fluorescence images of MCF-7 cells incubated with three kinds of DNA nanotubes, and the corresponding MFI, nucleus is stained Hoechst33324. Scale bar: 5 μm.

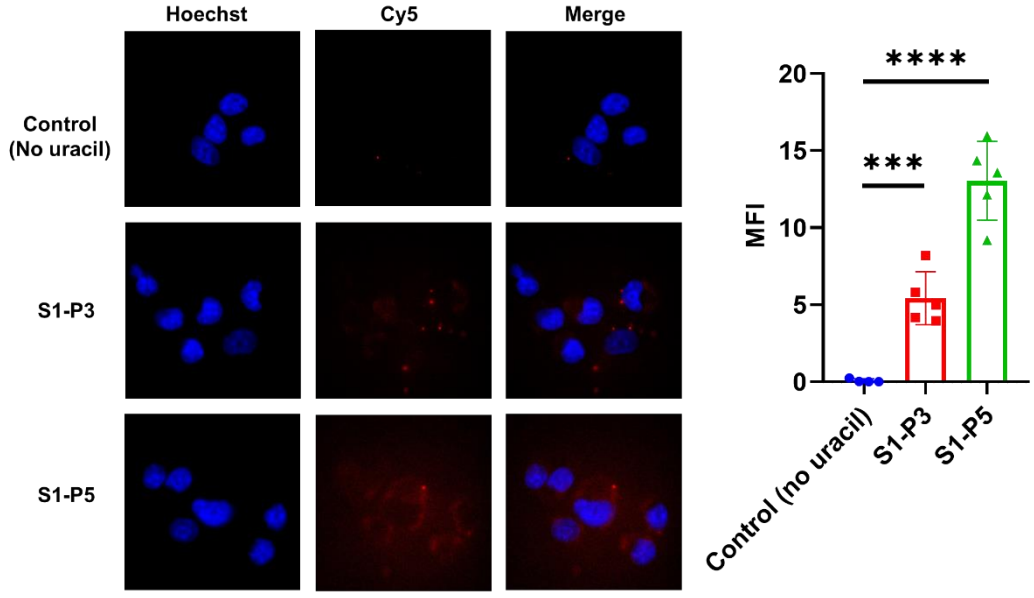

Figure S12. *HILO fluorescence images of A549 cells incubated with three kinds of DNA nanotubes, and the corresponding MFI, nucleus is stained Hoechst33324. Scale bar: 5 μm.*

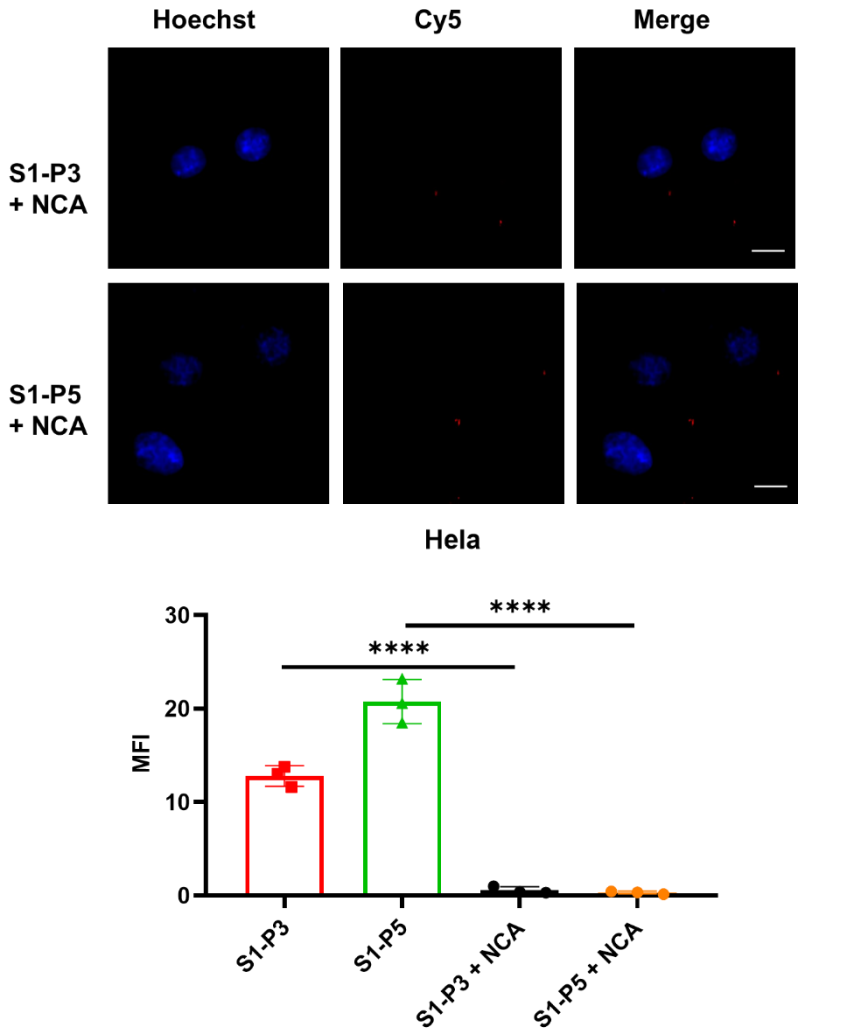

Figure S13. Fluorescence imaging of the NCA treated Hela cell with three kinds of DNA nanotubes, and the corresponding MFI. The nucleus was stained by Hoescht33342. Scale bar: 5 μm.

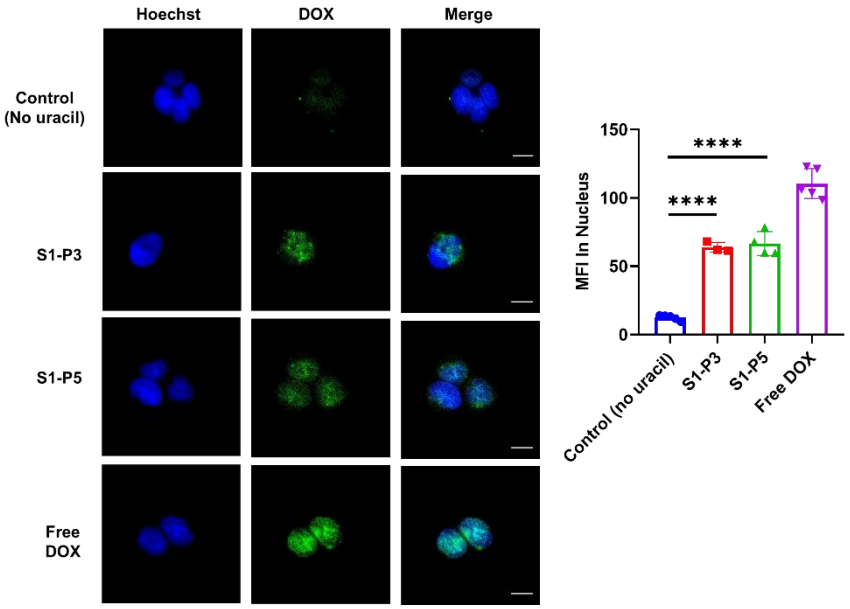

Figure S14. Exploring the cellular distribution of DOX (4 μM) which was carried by different vehicles in MCF-7 cell. MFI of nucleus is shown for each group. Scale bar: 5 μm

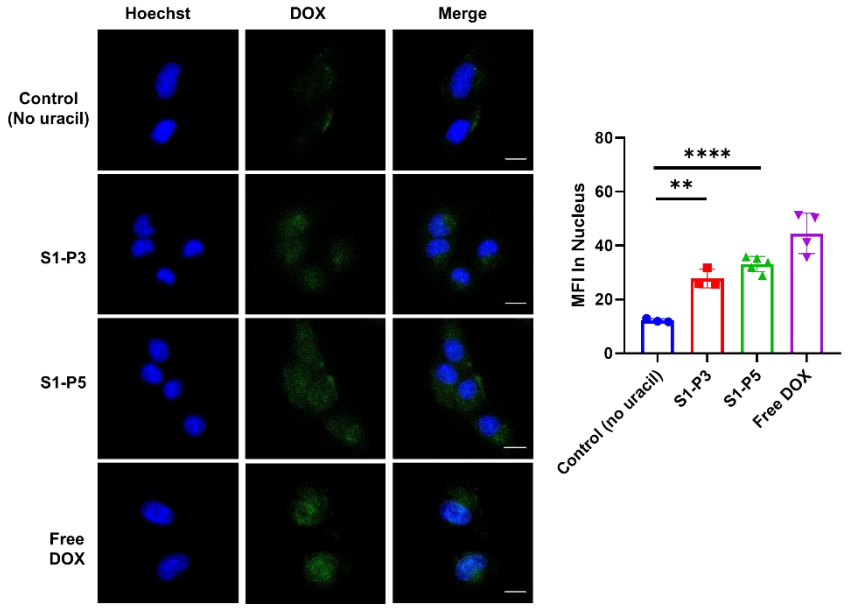

Figure S15. Exploring the cellular distribution of DOX (4 μM) which was carried by different vehicles in A549 cell. MFI of nucleus is shown for each group. Scale bar: 5 μm

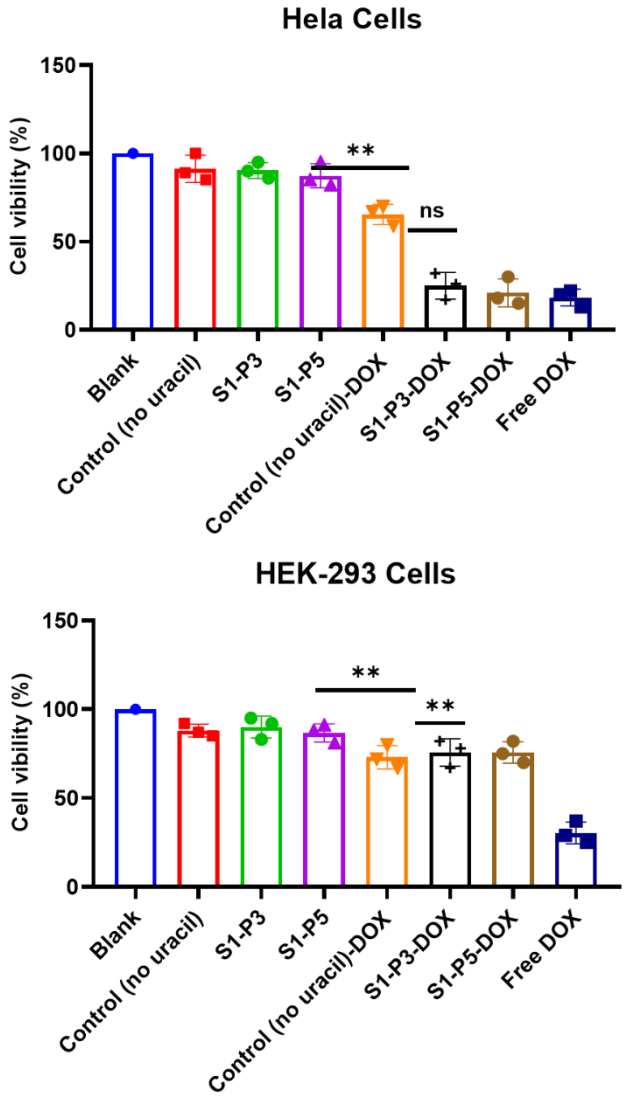

Figure S16. Cell viability measurement by CCK-8 kit. DOX concentration is 4 μM, and the nanotube concentration is 100 nM.

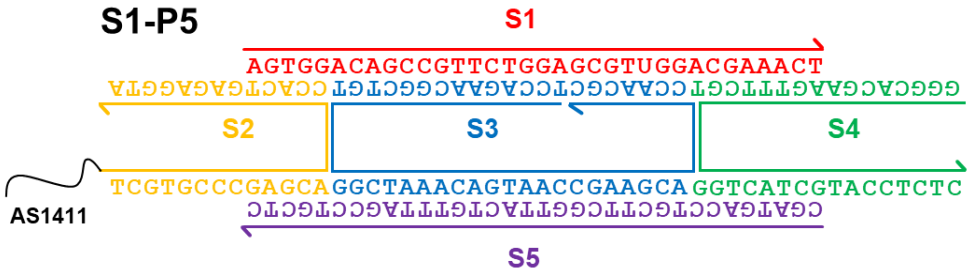

Figure 17. Scheme of AS1411 aptamer equipped uracil-containing DNA nanotube for in vivo drug delivery.

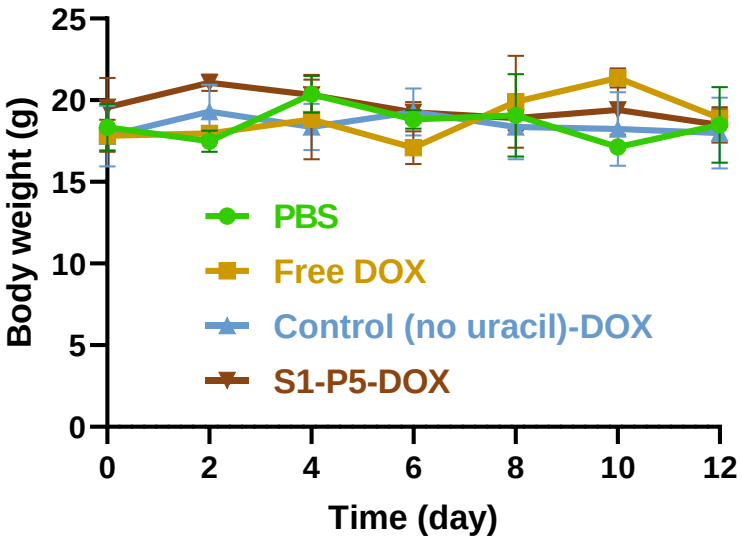

Figure S18. Body weight measurement of the mice from each group (n = 5) during the treatment.

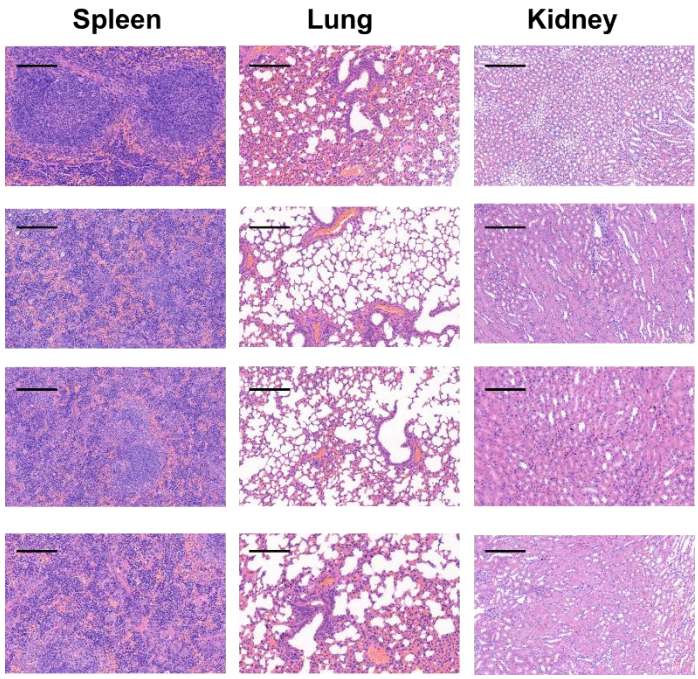

Figure S19. Histological examination of H&E stained slices of major organs (heart, liver, spleen, lung and kidney) after different treatments. Scale bar: 200 μm.

Supporting Tables

Table S1. Sequence of the oligonucleotides in this work.

Name	Sequence (5'-3')
S1 (no U)	AGTGGACAGCCGTTCTGGAGCGTTGGACGAAACT
S1-P1	AGTGGACAGCCGUTCTGGAGCGTTGGACGAAACT
S1-P2	AGTGGACAGCCGTUCTGGAGCGTTGGACGAAACT
S1-P3	AGTGGACAGCCGTTCUGGAGCGTTGGACGAAACT
S1-P4	AGTGGACAGCCGTTCTGGAGCGUTGGACGAAACT
S1-P5	AGTGGACAGCCGTTCTGGAGCGTUGGACGAAACT
S3-Cy5	Cy5-CCAGAACGGCTGTGGCTAAACAGTAACCGAAGCACCAACGCT
S4-BHQ3	GGGCACGAAGTTTCG/iBHQ3dT/GGTCATCGTACCTCTC
S2-AS1411	GGTGGTGGTGGTTGTGGTGGTGGTGGTTTTTTTTCGTGCCCGAGCACCACT GAGAGGTA

Table S2 Parameter setup of oxDNA simulation

Simulation type	Temperature	Simulation steps	Print configuration interval	Type	Hydrogen bond strength
Molecular dynamics (MD)	310 K	10^7	150000	60%	HYDR_A_T= 0.53122 HYDR_T_A = 0.53122 HYDR_C_G = 0.73942 HYDR_G_C = 0.73942
				70%	HYDR_A_T = 0.67288 HYDR_T_A = 0.67288 HYDR_C_G = 0.93660 HYDR_G_C = 0.93660
				80%	HYDR_A_T = 0.70829 HYDR_T_A = 0.70829 HYDR_C_G = 0.98590 HYDR_G_C = 0.98590
				87%	HYDR_A_T = 0.77027 HYDR_T_A = 0.77027 HYDR_C_G = 1.07216 HYDR_G_C = 1.07216