Supporting information:

Multivalent aptamer-modified tetrahedral DNA nanocage demonstrates high selectivity and safety for anti-tumor therapy

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Table S1. DNA sequences.

Strands	DNA sequences
A	5-CGTATCACCAGGCAGTTGAGACGAACATTCCTAAGTCTGAAATTTATCACCCGCCATAGTAG-3
B	5-CGATTACAGCTTGCTACACGATTCAGACTTAGGAATGTTCGACATGCGAGGGTCCAATACCG-3
C	5-GTGTAGCAAGCTGTAATCGACGGGAAGAGCATGCCCATCCACTACTATGGCGGGTGATAAA-3
D	5-CTCAACTGCCTGGTGATACGAGGTGGGCATGCTCTTCCCGACGGTATTGGACCCTCGCATG-3
D-Cy5	5-CTCAACTGCCTGGTGATACGAGGTGGGCATGCTCTTCCCGACGGTATTGGACCCTCGCATG-Cy5
A'	5-CGTATCACCAGGCAGTTGAGACGAACATTCCTAAGTCTGAAATTTATACCCGCCATAGTAGTTTTTTTGCAGTTGATCCTTTGGATACCCTGG-3
B'	5-CGATTACAGCTTGCTACACGATTCAGACTTAGGAATGTTCGACATGCGAGGGTCCAATACCGTTTTTTTGCAGTTGATCCTTTGGATACCCTGG-3
C'	5-

CGTGTAGCAAGCTGTAATCGACGGGAAGAGCATGCCCATCCACTACTATGGCGGGTGATAAATTTTTTTGCAGT TGATCCTTTGGATACCCTGG-3

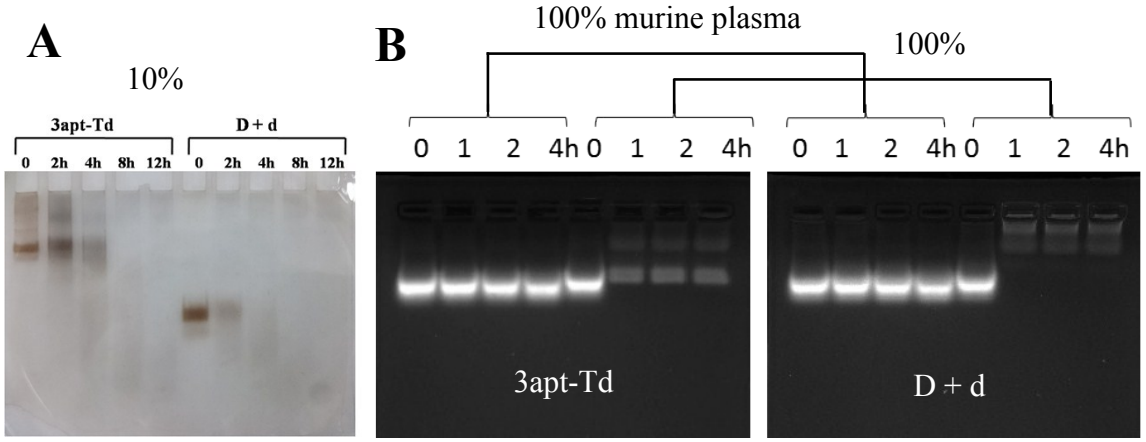

Figure S1. (A) Non-denaturing PAGE and (B) AGE analysis of the stability of 3apt-Td nanostructure. Totally complementary DNA duplex (strand D＋d) and 3apt-Td nanostructure were incubated in 10% non-heat inactivated FBS, 100% non-heat inactivated FBS and 100% murine plasma at 37 ^{o}C for 2-12 h and then analyzed with gel electrophoresis.

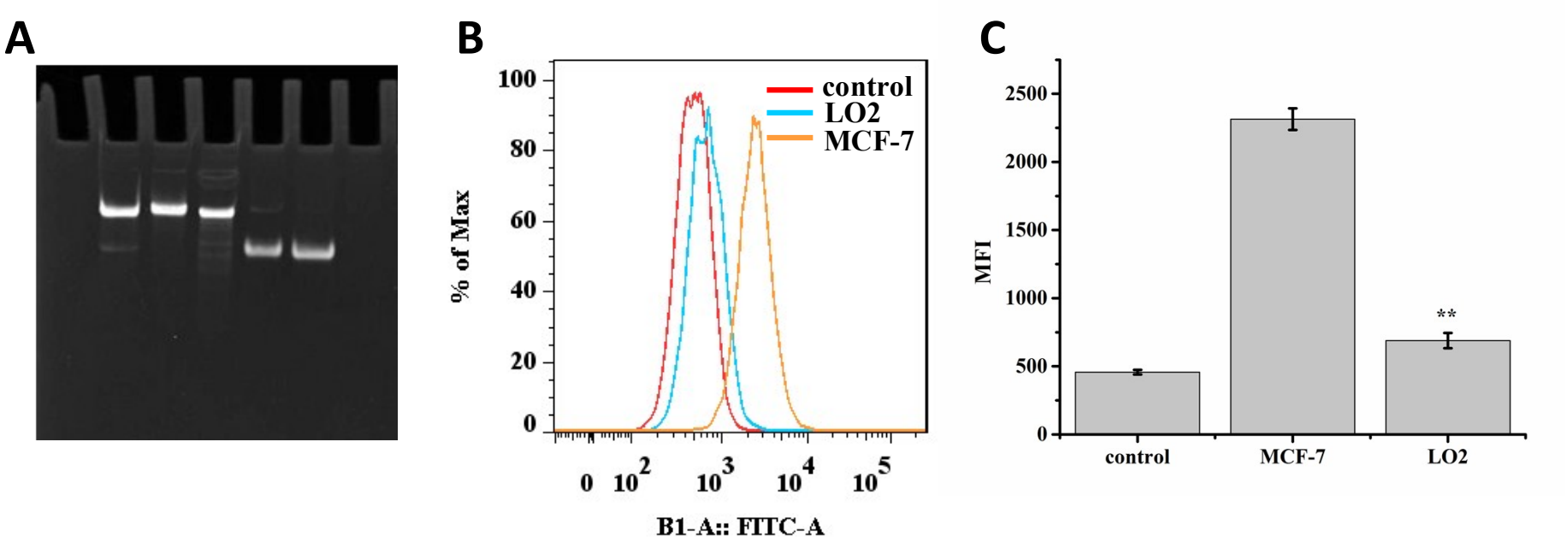

Figure S2. AGE gel (12%) shift assay (A) of B' stand containing aptamer sequence (B-7T-apt) incubated with the MUC1 peptide. These strip indicated B' strand, B' strand incubated with MUC1, B' strand incubated with BSA, d strand (DNA strand complementary with D strand) with

MUC1 and d strand. The flow cytometry ananlysis (B) and the mean fluorescence intensity (MFI; C) of MCF-7 and LO2 cells after incubation with the fluorescently labelled B' stand for 5 h. Data are shown as the mean ± SD (n = 3). ** indicates $p < 0.01$ versus MCF-7 cells.

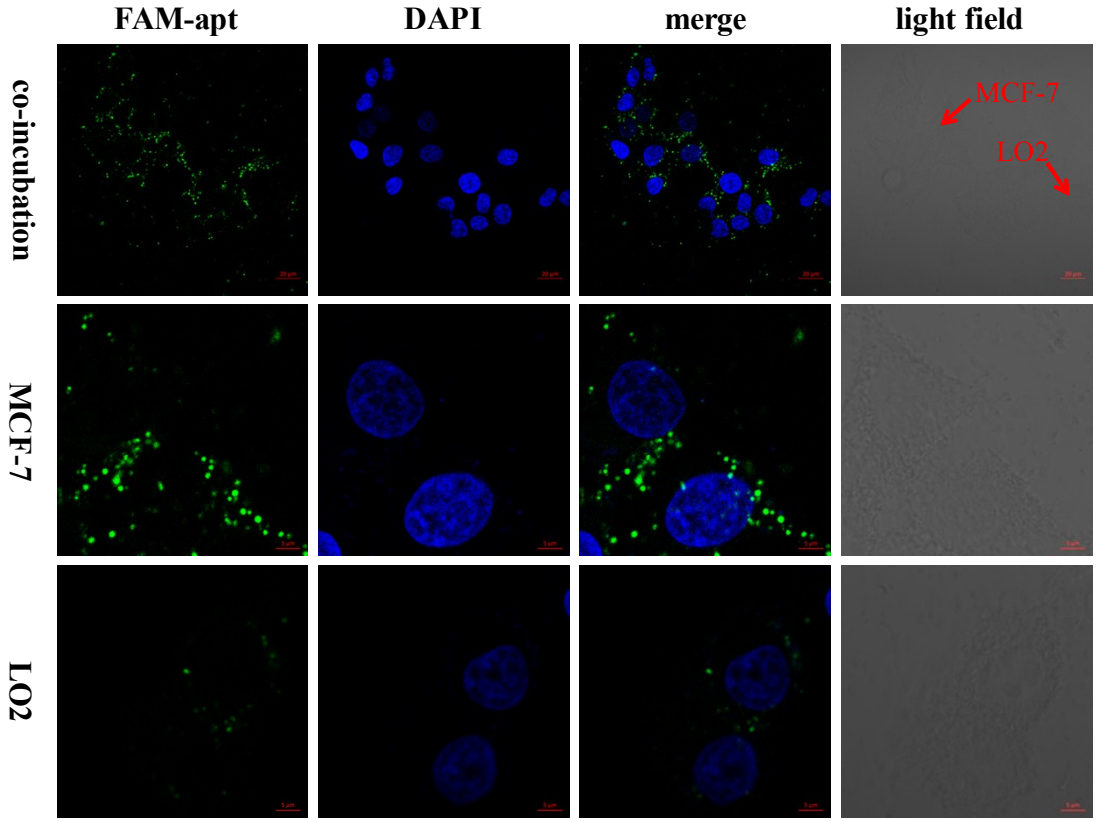

Figure S3. The cellular uptake of B' stand containing aptamer sequence (B-7T-apt) in MCF-7, LO2 cells and co-incubation cells after 5 h analyzed by confocal laser scanning microscopy.

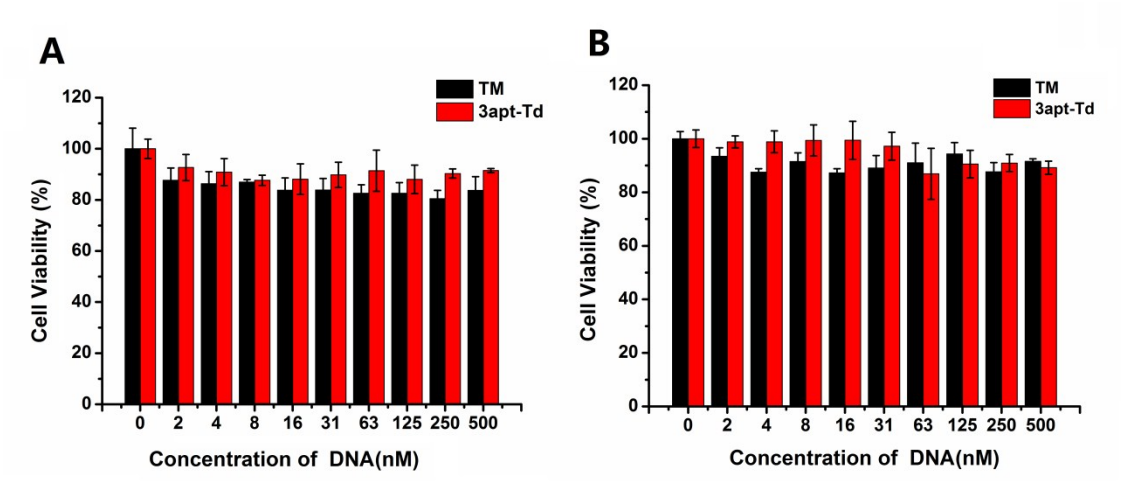

Figure S4. *In vitro* cytotoxicity assay of 3apt-Td against MCF-7(A) and LO2 cell lines (B) over 48 h.

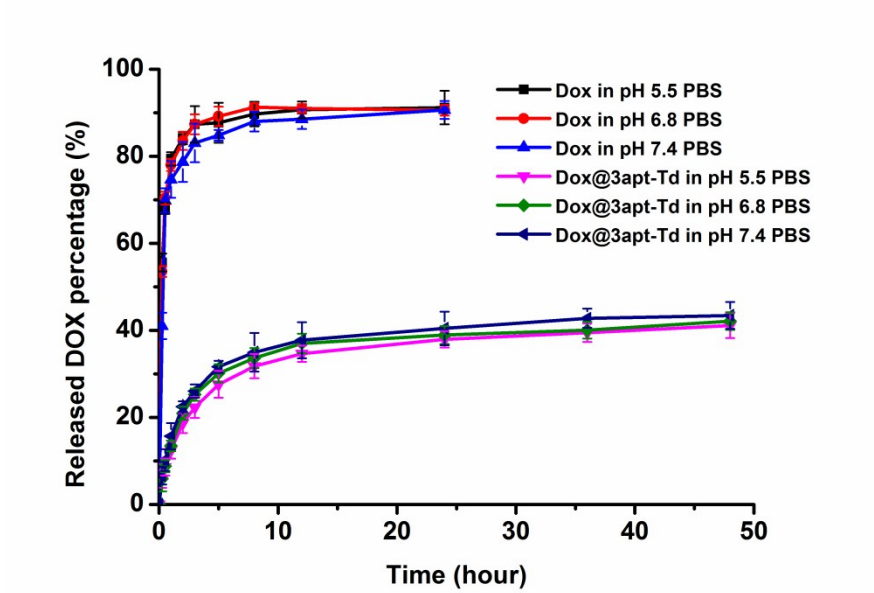

Figure S5. *In vitro* drug release profiles: Dox@Td and free Dox in PBS buffers with various pH values. Data are shown as the mean ± SD (n = 3).

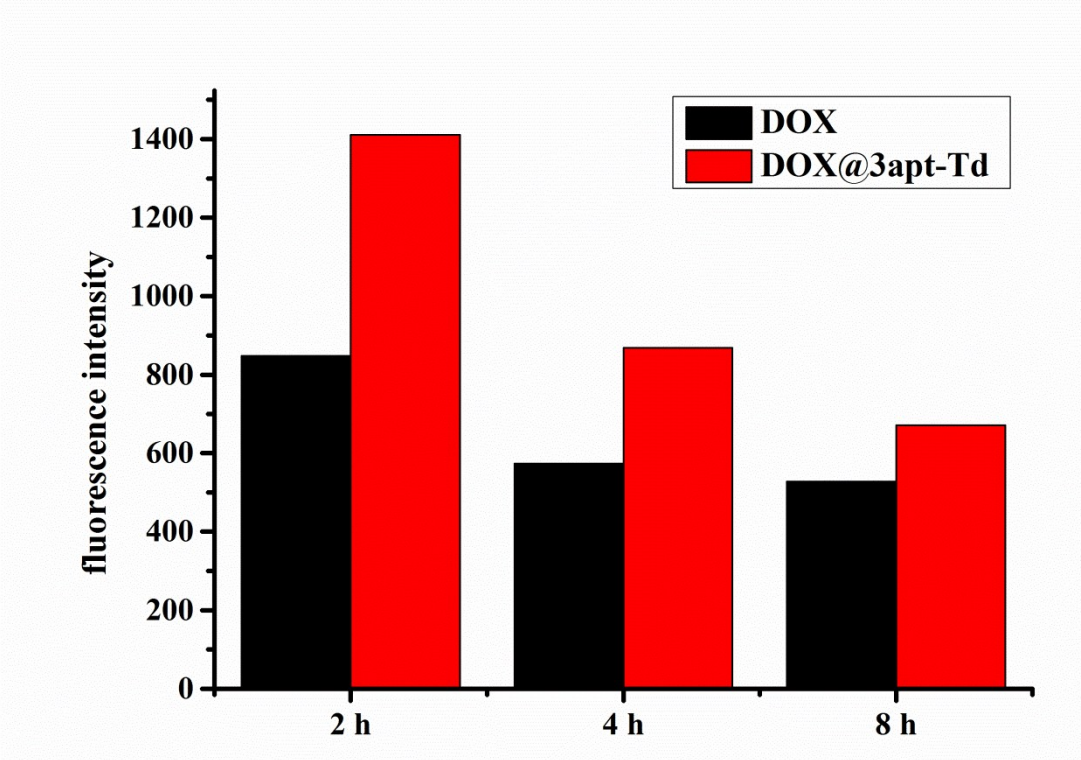

Figure S6. Quantification of DOX signal for the fluorescence microscopy images in MCF-7 tumor-bearing nude mice after intravenous injection of Dox (control) and Dox@3apt-Td.

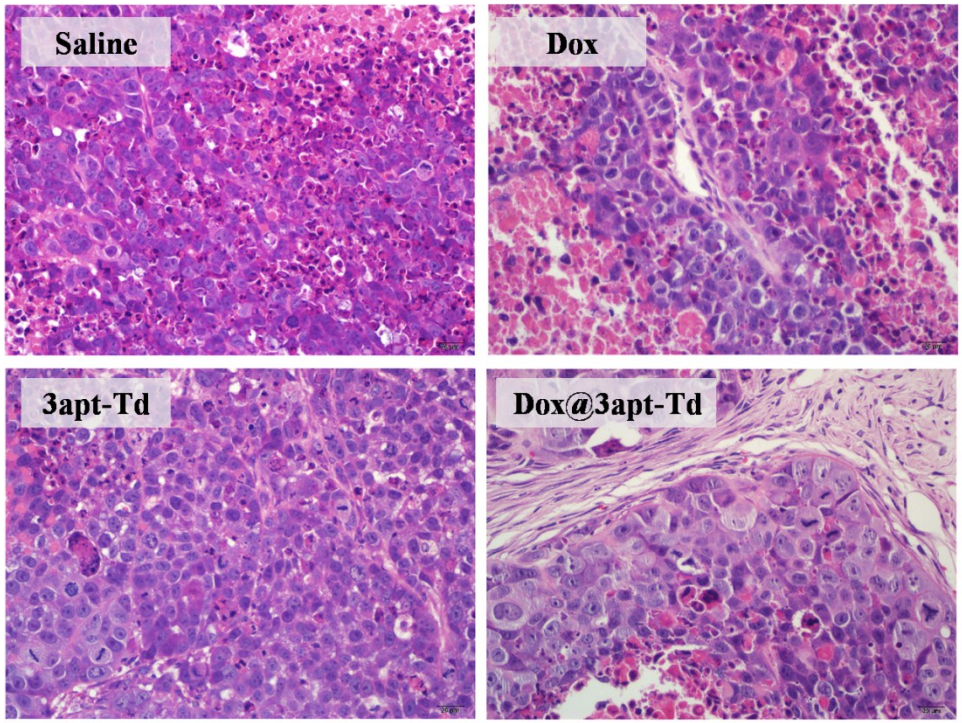

Figure S7. Histological changes of tumors dissected from nude mice bearing MCF-7 breast tumors treated with saline, 3apt-Td,free Dox and Dox@3apt-Td (Dox dose = 2 mg/kg). Histological analysis was performed via H&E staining, andthe images were observed by optical microscopy (Olympus, 400×).

Table S2. Effects of Dox on WBC count and spleen indices of MCF-7 tumor-bearing nude mice.

Groups	WBC count $\times 10^9(L^{-1})$	Spleen index (mg/g)
Saline	3.67 ± 0.15	0.73 ± 0.11
Dox	2.07 ± 0.57*	0.60 ± 0.03*
3apt-Td	2.52 ± 0.87	0.71 ± 0.09
Dox@3apt-Td	2.70 ± 0.98	0.73 ± 0.12

Table S3 The influence of the feeding molar ratio of 3apt-Td to Dox on the encapsulation efficiency (EE) and the number of Dox loaded in per 3apt-Td (n = 3).

Feeding molar ratio of 3apt-Td:Dox	EE (%)	Number of Dox loaded in per 3apt-Td
1 : 25	83.52 ± 8.12	20.88 ± 2.03
1 : 50	80.94 ± 5.26	40.47 ± 2.63
1 : 75	71.55 ± 4.71	53.66 ± 3.53
1 : 100	55.99 ± 7.88	55.99 ± 7.88