Supporting Information

Supramolecular DNA Nanogel through Host-guest Interaction of Cucurbit[8]uril for Targeted Drug Delivery

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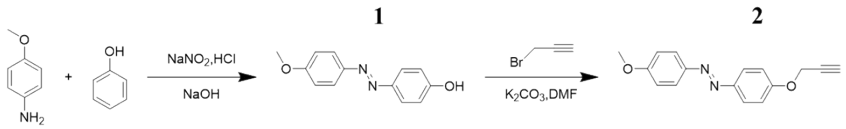
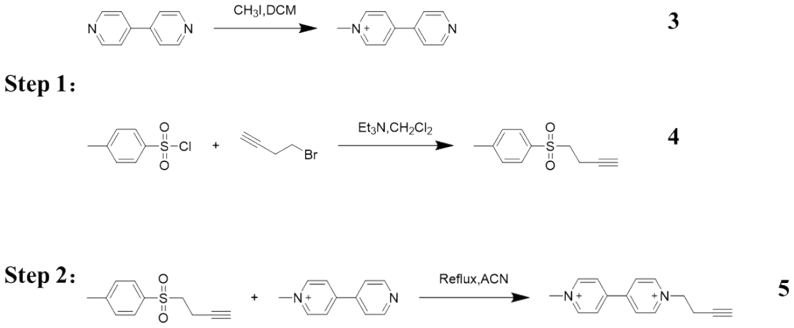


Scheme S1 Synthetic route of Azo.



Scheme S2 Synthetic route of MV.

Synthetic of Azo-alkynyl (2)[1]

6.15 g (50 mmol) p-methoxyaniline was dissolved in 125 mL 1 mol/l HCl solution. Then 3.795 g (55 mmol) $NaNO_2$ was dissolved in as little water as possible and slowly dropped into the above solution at 0 ° C, ice bath reaction for 1 h. Then, 4.4 g (110 mmol) NaOH was dissolved in 165 mL water and 5.17 g (55 mmol) phenol was added, and this solution was dropped into the previous solution and reacted in ice bath for 3 h. After the reaction was finished, the pH of the solution was adjusted to 3 (the color of the solution changed obviously), and the precipitate was filtered, washed and dried to obtain the intermediate product **1** p-methoxyazophenol.

2.28 g (10 mmol) of p-methoxyazophenol, 1.79 g (15 mmol) of bromopropyne were dissolved in 200 mL DMF, 1.59 g of K_2CO_3 (15 mmol) was added, and the amount of KI was added, 80 °C for 24 hours. The crude product was purified by column chromatography over silica gel (Petroleum ether: ethyl acetate = 3:1) to obtain the pure product **2** (Azo-alkynyl).

Synthetic of MV-alkynyl (5)[2]

Mixture of 4,4'-bipyridine (3.12 g, 20 mmol) and methyl iodide (2.84 g, 20 mmol) in 100 mL CH_2Cl_2 was refluxed and stirred for 12 h. The crude product was recrystallized in CH_2Cl_2 to obtain the pure product **3**.

A mixture solution of 3-butyn-1-ol (3.24 mL, 42.8 mmol) and triethylamine (7.7 mL, 55.4 mmol) in 15 mLCH_2Cl_2 were slowly dropped into 15 mL CH_2Cl_2 with 8.97 g (47 mmol) 4-toluenesulfonyl chloride in ice bath. After one night reaction at r.t., 30 mL water was added and stirred for 20 min. The quenched solution was extracted with CH_2Cl_2 (3×40 mL), the organic layer was collected and washed with 60 mL saturated sodium

chloride solution, dried over Na_2SO_4 and evaporated to get red oil **(4)**.

0.3 g (1 mmol) **3** and 0.672 g (3 mmol) **4** were dissolved in 5 mL acetonitrile, 90 ℃ reflux for 60 h. The solvent was evaporated and the resident was washed with ether (3×20 mL) and acetone(3×20 mL). The product was dissolved in acetonitrile and added to the violently stirred acetone, centrifuged and dried to obtain the dark green product. Obtaining chloride salt product **5** from sulfonate product through salt exchange operation.

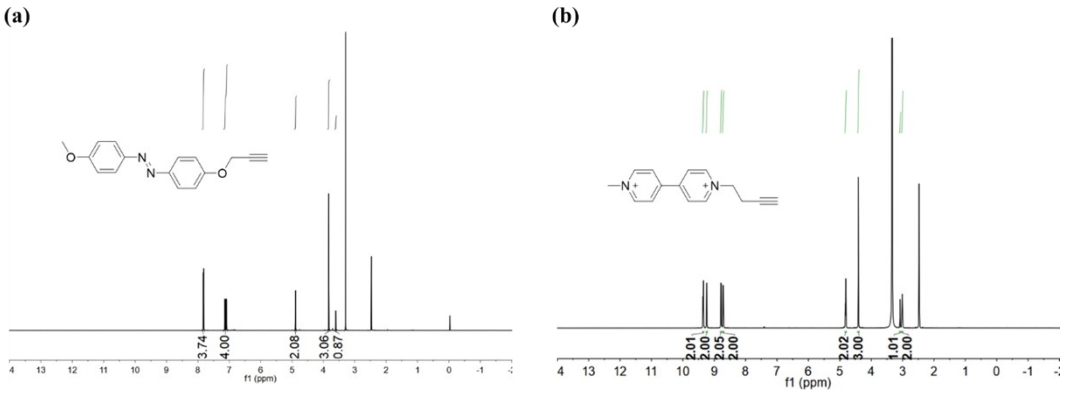
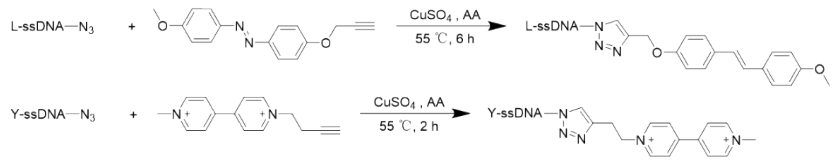


Figure S1 (a) ^{1}H NMR spectrum (600 MHz, DMSO-d6, 298 K) of Azo. (b) ^{1}H NMR spectrum (600 MHz, DMSO-d6, 298 K) of MV.

(a)



(b)

Name	Sequence:5' to 3'
ssDNA1-N_3	N_3-TAC TAC ACC ACC ACA ACA
ssDNA2-N_3	N_3-TGT TGT GGT GGT GTA GTA
ssDNA3-N_3	N_3-CAG TAC TAT GCT CAC CAC GGA GGA ACT C
ssDNA4-N_3	N_3-GAG TTC CTC CGA GGT CAT TCT CGA CAA G
ssDNA5-N_3	N_3-CTT GTC GAG AAT GAT GAG CAT AGT ACT G
ssDNA3-Apt	GCA GTT GAT CCT TTG GAT ACC CTG G CAG TAC TAT GCT CAC CAC GGA GGA ACT C

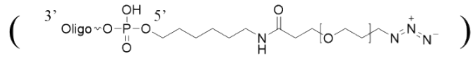


Figure S2 (a) Modify the guest molecule onto DNA by click reaction. (b) The sequence and structure of DNA.

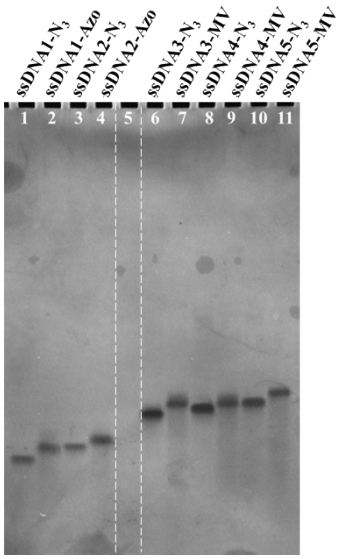


Figure S3 20% denature PAGE analyses of raw DNA and modified DNA.

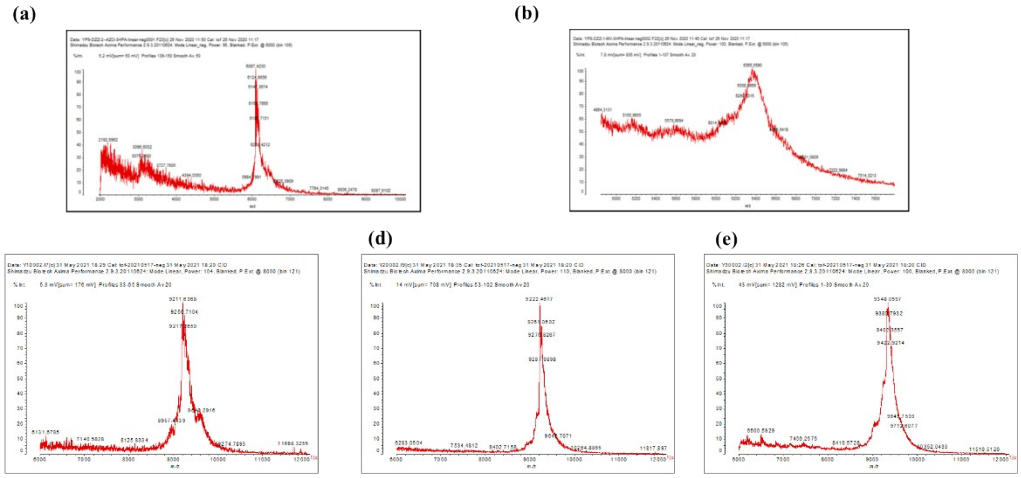


Figure S4

(a). Mass spectrum of ssDNA1-Azo (Calculated value:6085; Actual value:6087.4230);

(b) Mass spectrum of ssDNA2-Azo (Calculated value:6351; Actual value:6365.5590) ;

(c). Mass spectrum of ssDNA1-MV (Calculated value:9211; Actual value:9211.6368);

(d). Mass spectrum of ssDNA2-MV (Calculated value:9242; Actual value:9222.4617);

(e). Mass spectrum of ssDNA3-MV (Calculated value:9345; Actual value:9348.0597).

Table S1 DNA building units concentration and proportion during supramolecular DNA nanogel assembly process.

	Y-3M (μM)	Y-1M (μM)	L-2Azo (μM)	CB[8] (μM)
eq	3	1	5	10
SDN-1	0.3	0.1	0.5	1
SDN-2	0.6	0.2	1	2
SDN-3	0.9	0.3	1.5	3
SDN-4	1.2	0.4	2	4

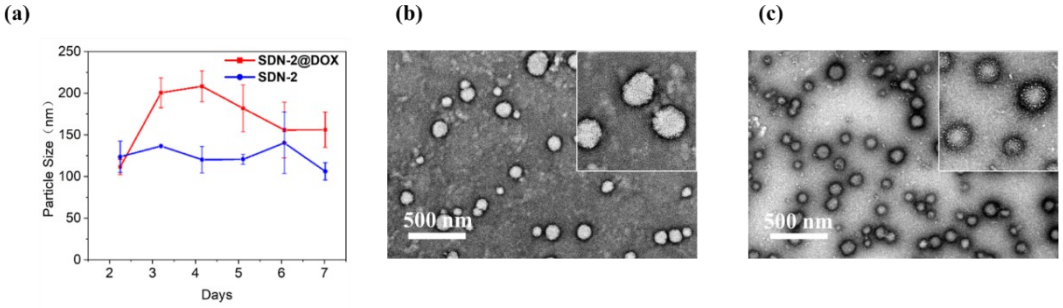


Figure S5 (a) DLS data of SDN-2 in a week;(b) TEM image of SDN-2 after incubation for one week;(c) TEM image of SDN-2@DOX after incubation for one week. Scale bar: 500 nm.

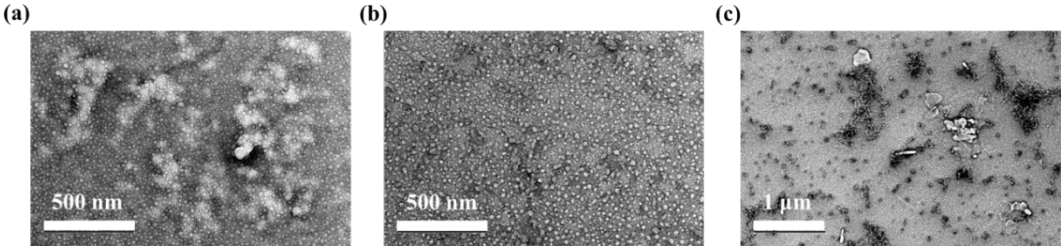


Figure S6 (a) TEM images of SDN-2 under UV light irradiation for 30 min. (b) TEM images of SDN-2 under UV light irradiation for 60 min. (c) TEM images of SDN-2 and FGG peptides co incubated for 1 h.

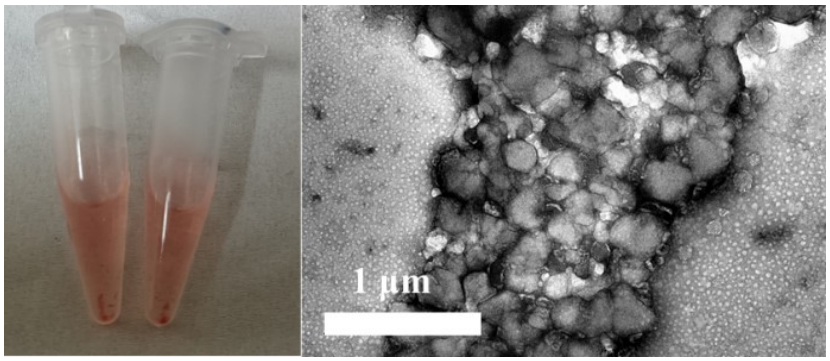


Figure S7 SDN-2@DOX obtained by high-speed centrifugation.

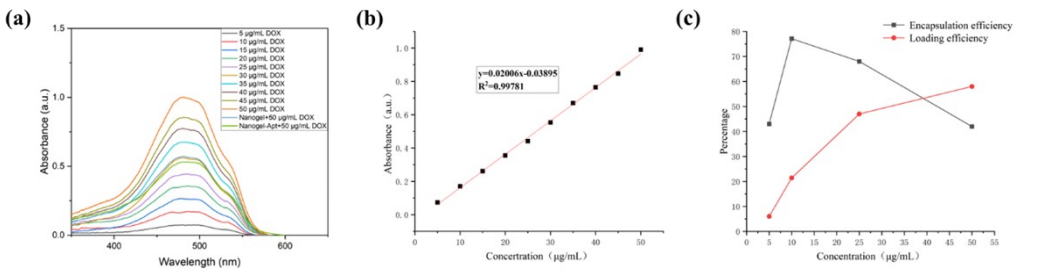


Figure S8 (a) UV-Vis absorption of DOX; (b) UV-Vis absorption standard curve of DOX; (c) Changes of drug encapsulation efficiency and loading efficiency with different drug concentration

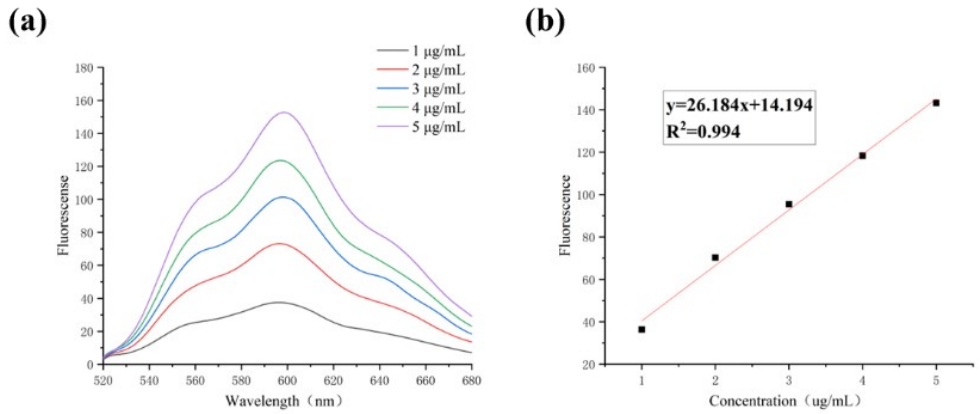


Figure S9 (a)Fluorescent changes of DOX (1-5 ug/ml); (b) Fluorescence standard curve of DOX

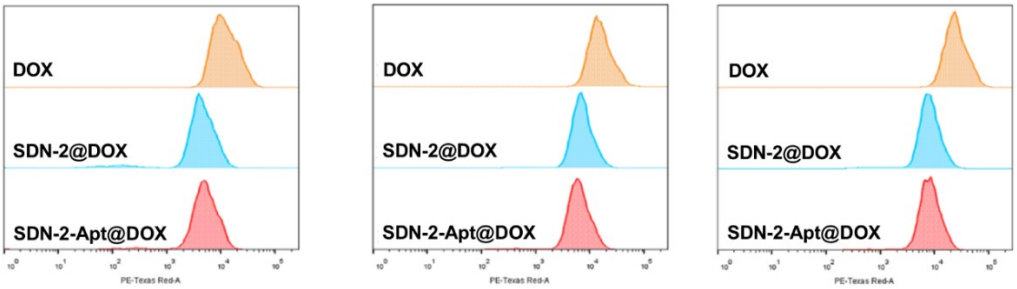


Figure S10 Flow cytometry analysis of the targeting ability of DOX，SDN-2@DOX and SDN-2-Apt/ DOX in MDA-MB-231 cells at different incubation time (a) 2 h, (b) 4 h, (c) 6 h.

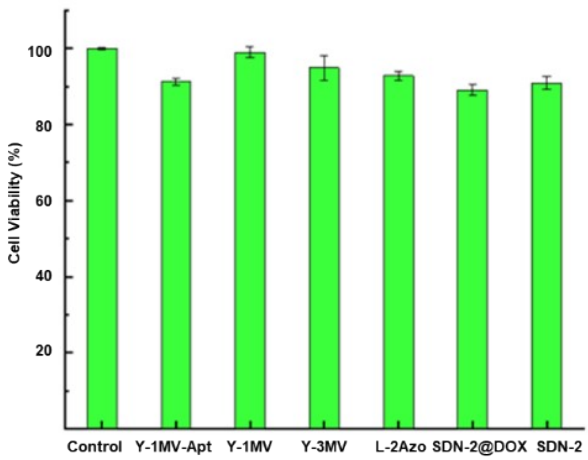


Figure S11 In vitro cytotoxicity of DNA building units and SDN-2 in MCF-7 cells.

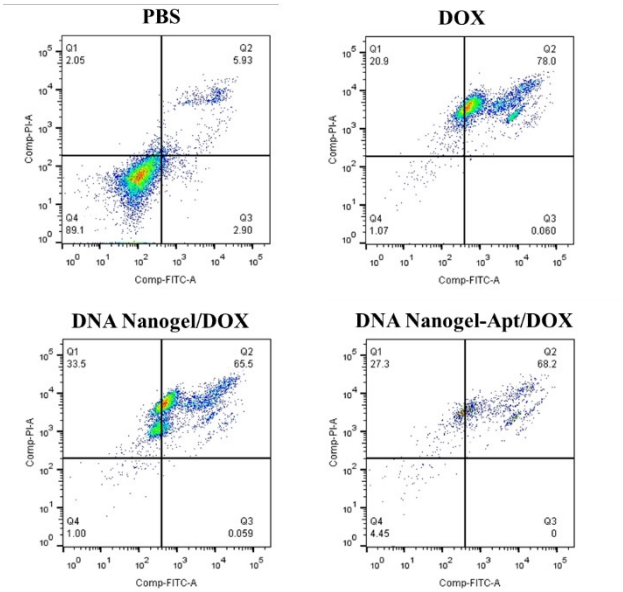


Figure S12 Apoptosis assay of the MDA-MB-231cells treated with DOX，SDN-2@DOX and SDN-2-Apt@ DOX (DOX Concentration: 5 μM).

Notes and references

[1] Z. Cheng, S. Ma, Y. Zhang, S. Huang, Y. Chen and H. Yu, Photomechanical Motion of Liquid-Crystalline Fibers Bending Away from a Light Source, Macromolecules, 2017, 50, 8317–8324.

[2] H.-B. Bu et al, Efficient post-polymerization functionalization of conducting poly(3,4-ethylenedioxythiophene) (PEDOT) via 'click'-reaction, Tetrahedron, 2011, 67, 1114-1125.