Supporting Information

Aptamer-functionalized fluorine-containing DNAsome for targeted drug delivery to cancer cells

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1. Experimental section

(1) Synthesis of compound 1

4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11 Heptafluorodecyl iodide (1 g, 1.7 mmol), DIPEA (0.22 g, 1.7 mmol) and 4-aminophenol (0.083 g, 0.77 mmol) were mixed in anhydrous DMF solution (5 mL) under nitrogen protection and stirred at 120 °C under reflux overnight. After cooling to room temperature, the reaction mixture was poured into 50 mL of water, then extracted 3 times with 100 mL of EtOAc. The collected organic phase was dried over anhydrous Na_2SO_4 and concentrated under low pressure. After purification by flash chromatography (hexane to 20/80 EtOAc/hexane), ~ 0.5 g of compound **1** was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (s, 1H), 6.77 (d, 2H), 6.75 (d, 2H), 3.17 (t, 4H), 2.13 (m, 4H), 1.78 (m, 4H).

(2) Synthesis of Compound 2

Compound **1** (0.5 g, 0.49 mmol) was dissolved in 20 mL of anhydrous dichloromethane, followed by addition of 0.19 g of DIPEA (1.47 mmol). After the mixture was cooled in an ice bath, 0.17 g of 2-cyanoethyl-N,N- diisopropylchlorophosphoramidite (0.73 mmol) was added. After removing the ice bath, the reaction was continued at room temperature with stirring for an

additional 2 h. Subsequently, the reaction mixture was successively washed with saturated $NaHCO_3$, brine, and water. The organic phase was collected, dried over anhydrous Na_2SO_4, and concentrated under low pressure. After purification by a flash chromatographic column, compound **2** of ~0.4 g was obtained. ^1H NMR (500 MHz, $CDCl_3$): δ 6.98 (d, 2H), 6.73(d, 2H), 3.92 (m, 2H), 3.75 (m, 2H), 3.24 (t, 4H), 2.65 (t, 2H), 2.12 (m, 4H), 1.82 (m, 4H), 1.18−1.25 (m, 12H). ^{31}P NMR (500 MHz, $CDCl_3$): δ 148.49.

(3) UV-vis characterization of compound 1 and the DNA amphiphilic compound

The optical properties of compound **1** and DNA amphiphilic compounds were measured using an UV-vis spectrometer, with a 2 nm slit width at a scan speed of 200 nm/min. The final solution were prepared to a concentration of 2 μM. Absorption spectra were recorded using quartz cuvette of 10 mm path length on a UV-750 Ultraviolet Spectrophotometer.

(4) *In vitro* releasing of DOX for DOX/DNAsomes on pH stimuli

Sgc8/DOX/DNAsomes (5 μM) in Tris buffer (pH 5.0 or 7.4) was continuously incubated at 37 ℃. At selected time intervals (2, 6, 12, 24 and 36 h), the fluorescence spectra of the solution with the exitation at 470 nm was determined to evaluate the amount of released DOX.

(5) Statistical Analysis

All experiment was conducted in triplicate. Data reported are mean ± standard deviation (SD). Otherwise stated differently, statistical significance was ascertained when $p < 0.05$ following the One tailed Student's t-test analysis.

Tabel S1. The DNA sequences used in this work.

Sgc8	5'-ATCTAACTGCTGCGCCGCCGGGAAAATACTGTACGGTTAGATTTTTTTGGGTGCGA-3'
2F-DNA	3'-ACCCACGCT-2(fluorinated alkyl chain)-5'
Cy5-Sgc8	5'-Cy5-ATCTAACTGCTGCGCCGCCGGGAAAATACTGTACGGTTAGATTTTTTTGGGTGCGA-3'

Underlined letters in three sequences are used for hybridizing to form the DNA duplex at the surface of the F-DNAsomes or DOX/DNAsomes.

Tabel S2. Comparison of Encapsulating efficiency of DOX for different nanocarriers.

Type of DNA amphiphile assembly	Encapsulating efficiency of DOX	References
Aptamer-decorated DNAsomes	82%	This work
	91%	1
DNA nanostructures	79%	2
Aptamer-DNA micelles	96.8	3
DNA-conjugated gold nanoprobes	34.9% (566 DOX molecules per probe)	4

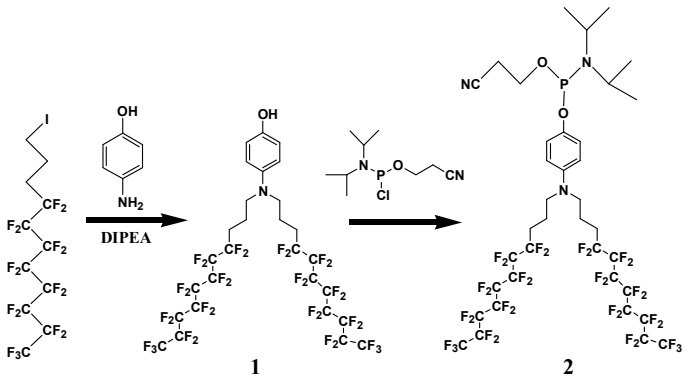


Fig. S1 Synthesis route of diperfluorodecyl phosphoramidite.

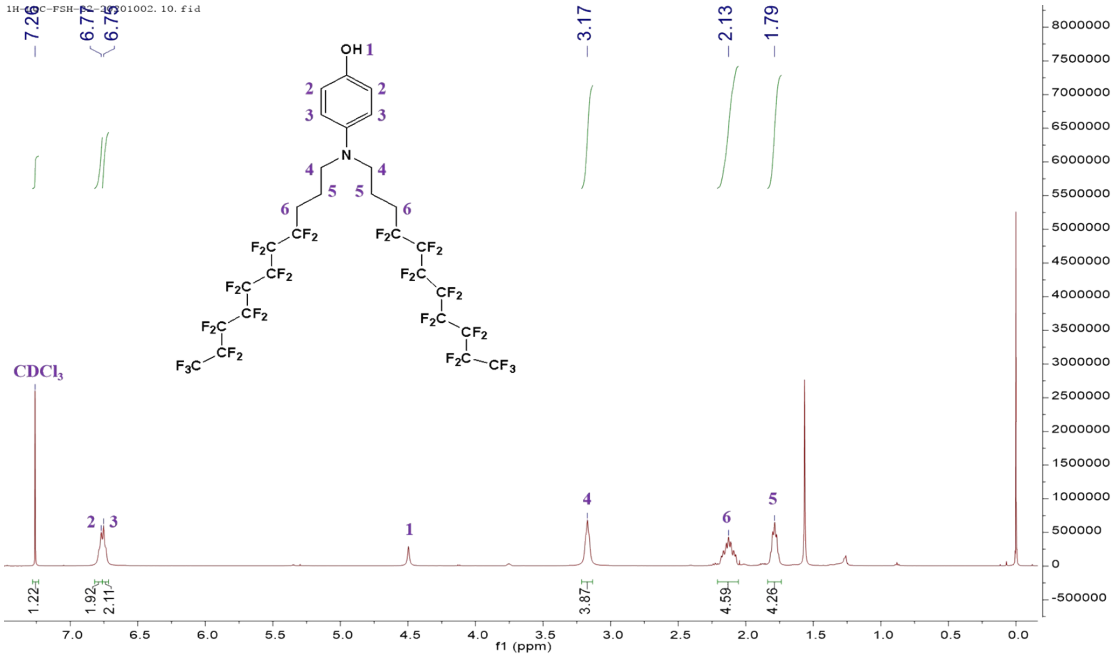


Fig. S2 ^{1}H NMR spectrum of compound **1.**

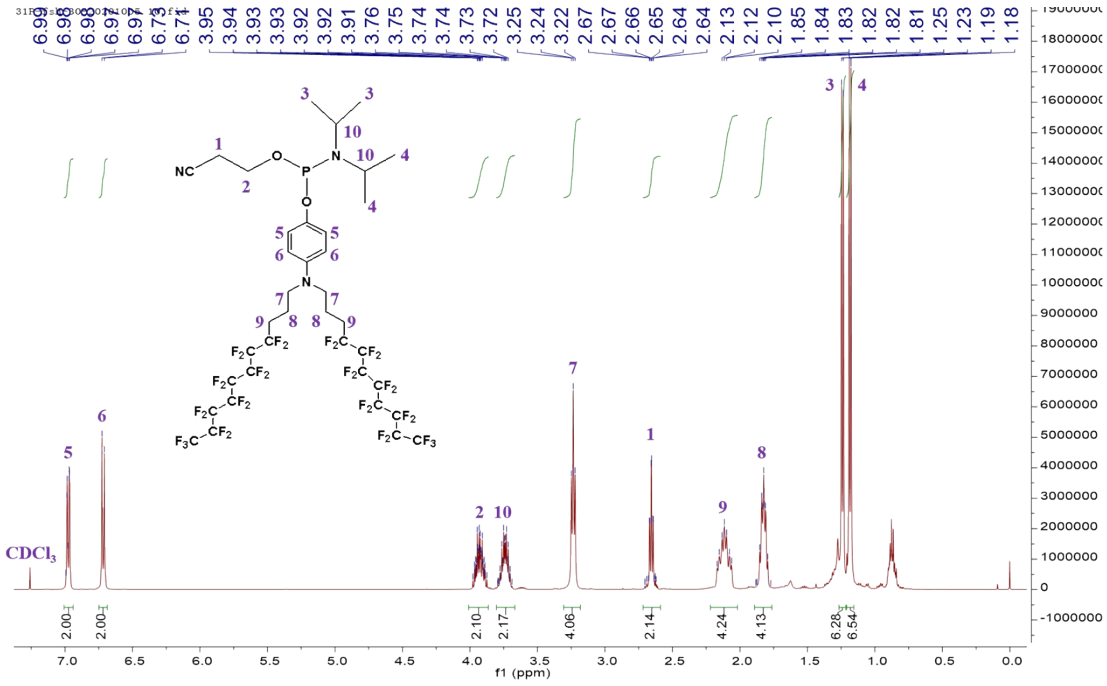


Fig. S3 ^{1}H NMR spectrum of compound **2.**

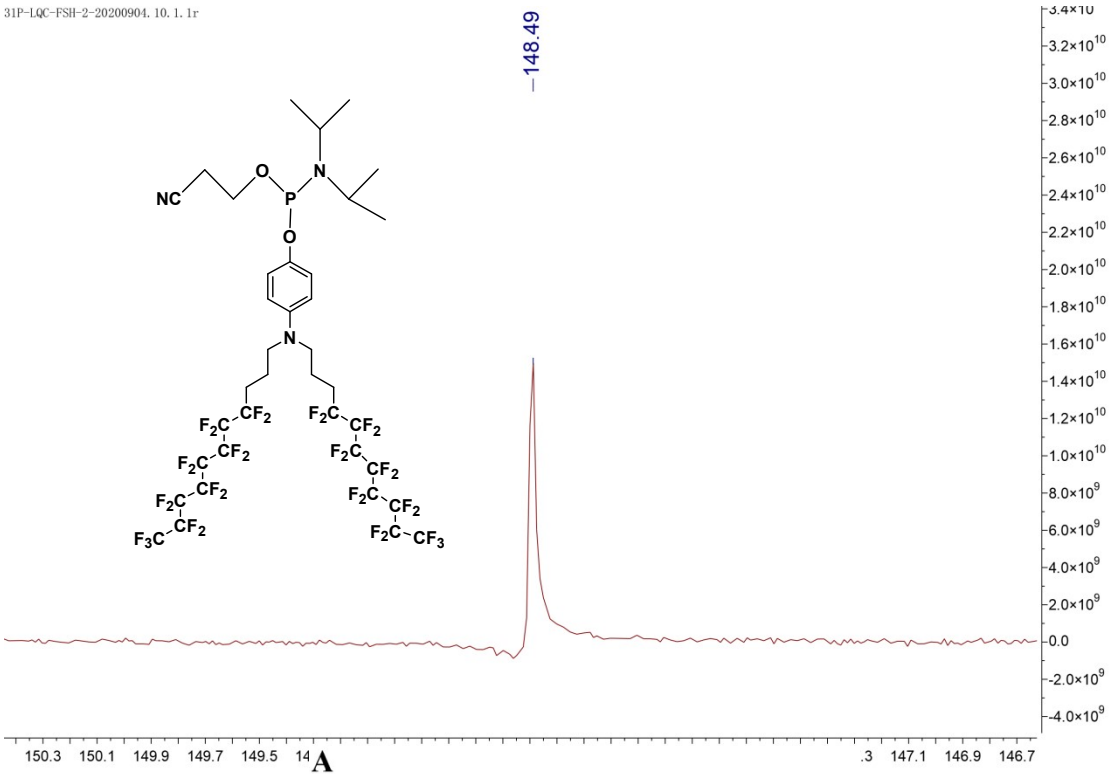
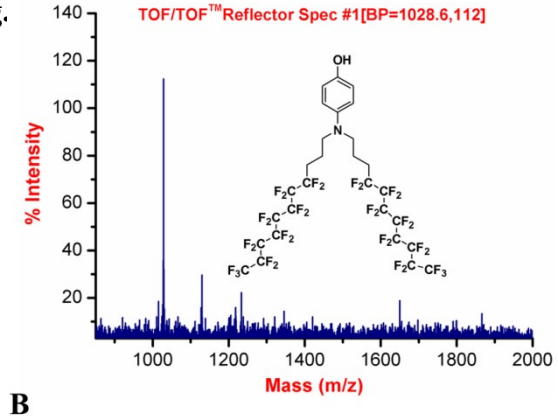


Fig.



B

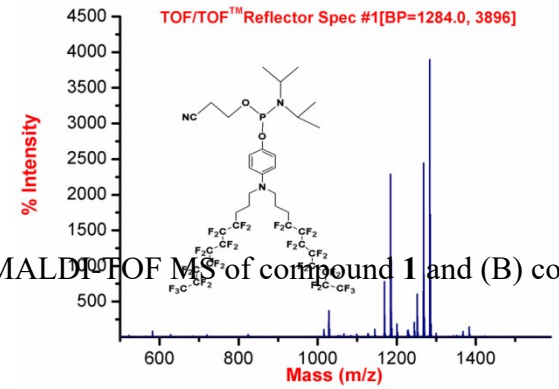


Fig. S5 (A) MALDI-TOF MS of compound **1** and (B) compound **2.**

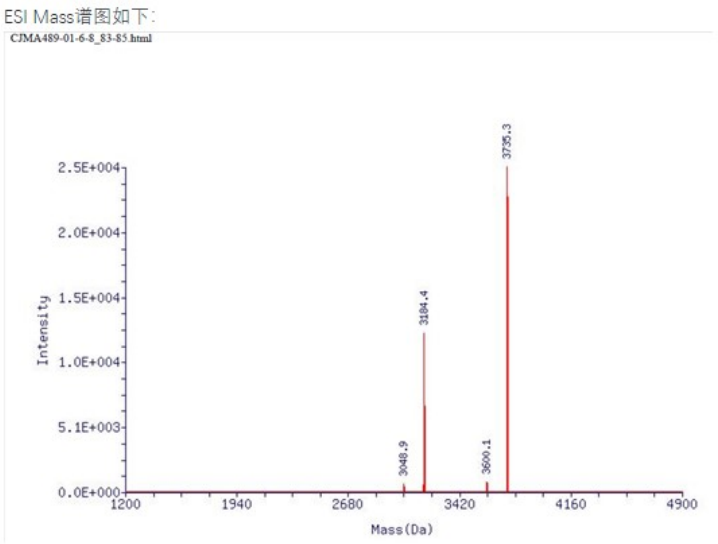


Fig. S6 ESI Mass spectrum of DNA amphiphilic compounds.

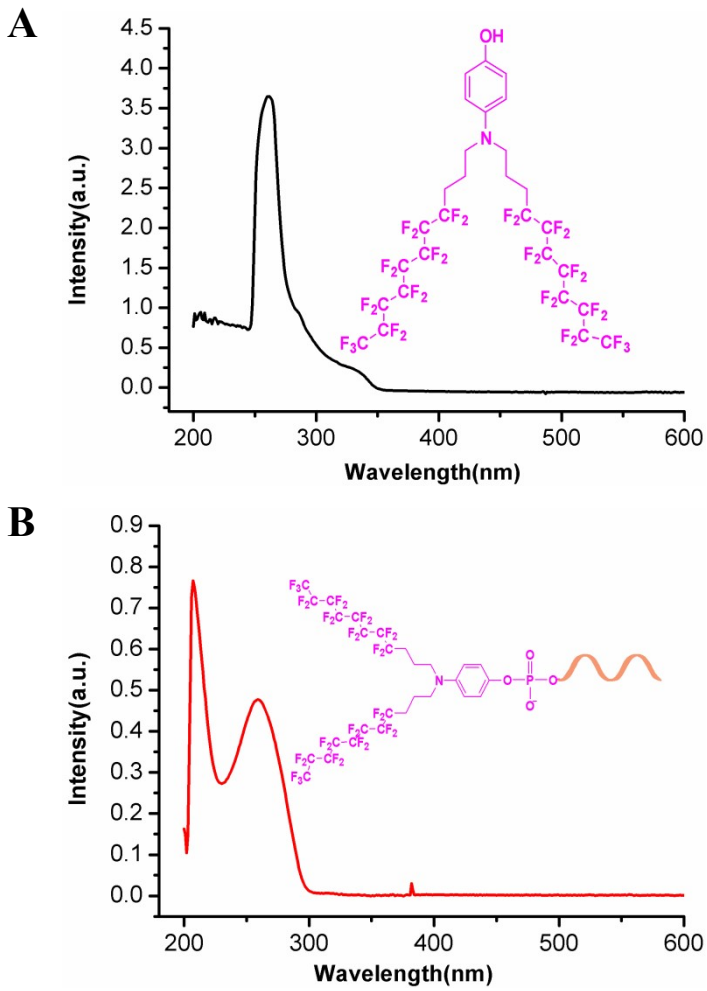


Fig. S7 UV-vis absorption spectrum (A) of compound **1** and (B) DNA amphiphilic compounds.

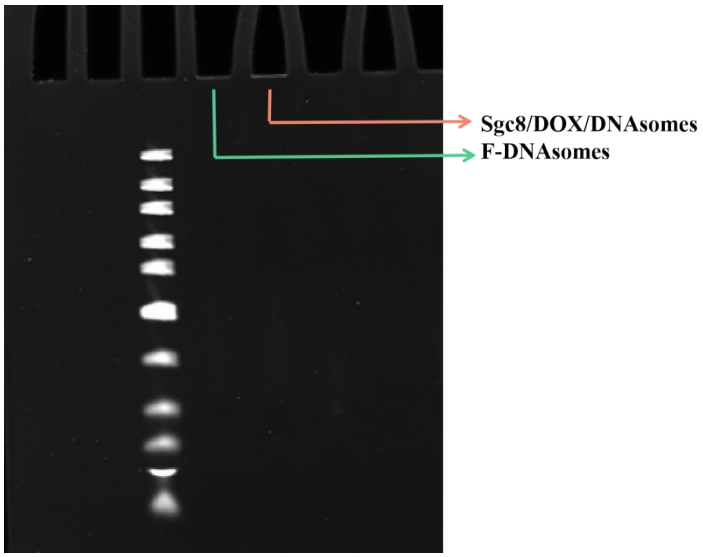


Fig. S8 Denaturing polyacrylamide gel (20%) of F-DNAsomes and Sgc8/DOX/DNAsomes after staining with ethidium bromide solution.

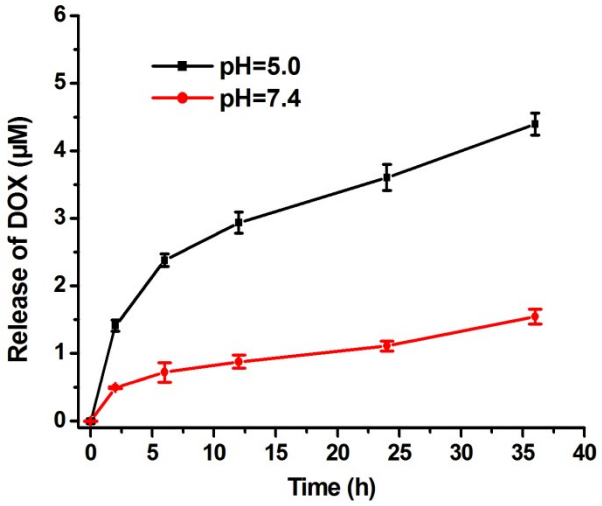


Fig. S9 The DOX release profiles of DOX/DNAsomes under different conditions (pH = 5.0 and 7.4).

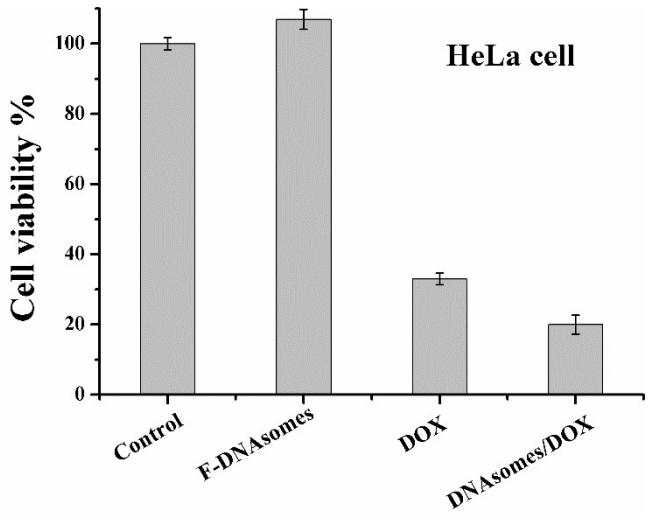


Fig. S10 MTT assay of HeLa cells treated with DOX and DOX/DNAsomes at 5 μM DOX concentration.

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3. R. Zhang, S. Gao, Z. Wang, D. Han, L. Liu, Q. Ma, W. Tan, J. Tian and X. Chen, *Adv Funct Mater*, 2017, **27**, 1701027.

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