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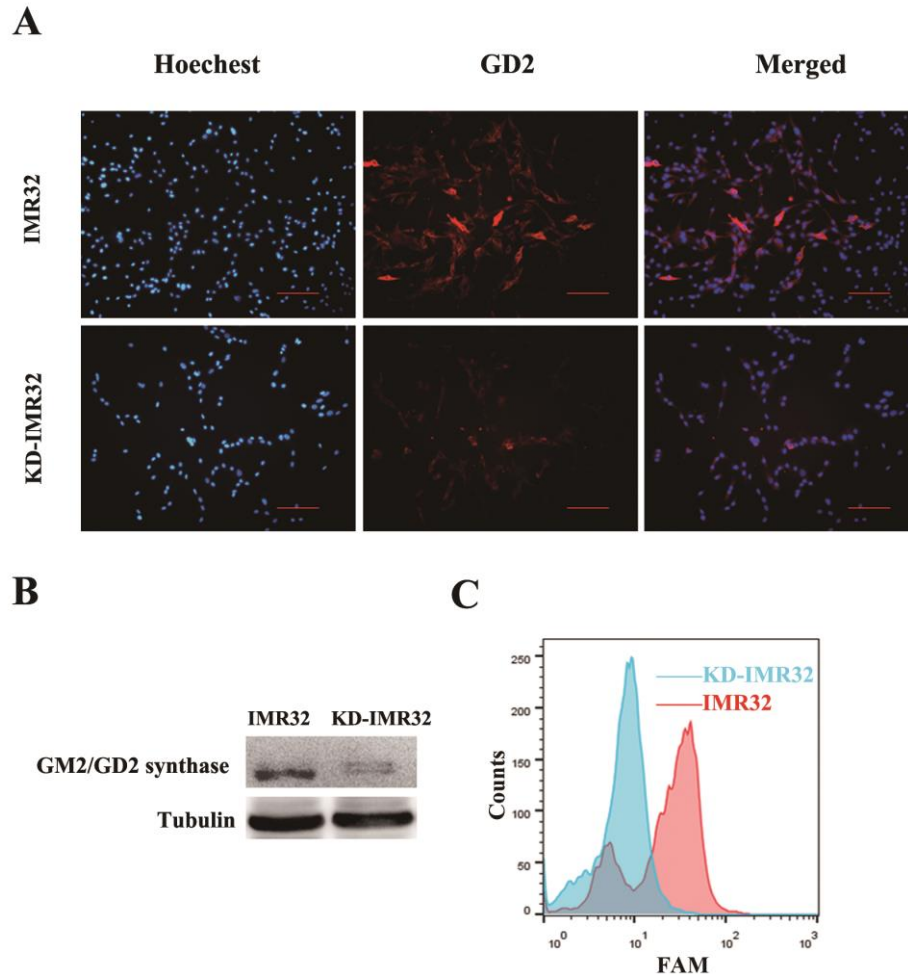
Supplemental information

A GD2-aptamer-mediated, self-assembling nanomedicine for targeted multiple treatments in neuroblastoma theranostics

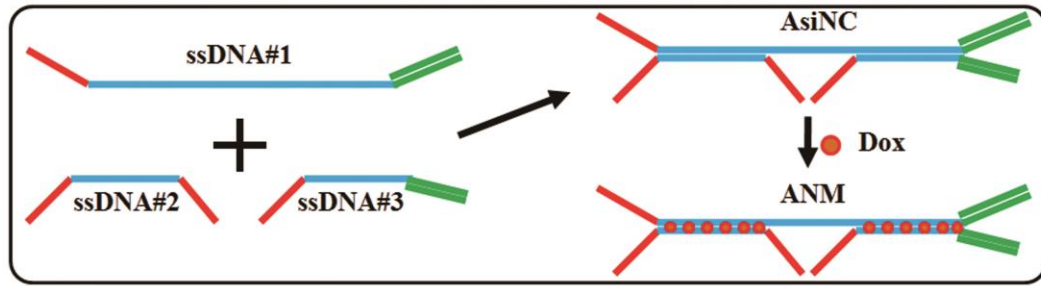
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Supporting Information

Supplementary figures:



Supplementary Figure 1. Knock down and evaluation of GM2/GD2 synthase in IMR32 cells. (A) Confocal microscope imaging indicated that KD-IMR32 cells expressed lower level of GD2 (Scale bar=50 μ M); (B) Evaluation of GM2/GD2 synthase expressed in IMR32 and KD-IMR32 by western blot; Tubulin was treated as internal reference gene. (C) The target confirmation of GD2 aptamer by flow cytometry.



ssDNA#1

5'-GD2 aptamer/Dox loading linker#1/MYCN siRNA#1

5'-CCGCCCAAATCCCTAAGAGCACAAACACCAACACAACCACCCCAACCAGACACACTACACACGCA^{CCCGGGCGCGCGCCCGC}
GGCCCGGGCGCGCGCCCGCGCGGAGTTGGTAAAGAATGA-3'

ssDNA#2

5'-GD2 aptamer/ Dox loading linker#2/GD2-aptamer-3'

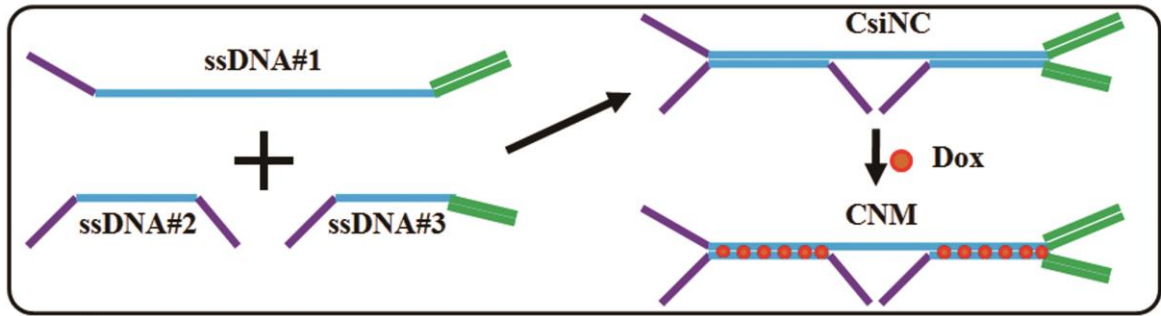
5'-CCGCCCAAATCCCTAAGAGCACAAACACCAACACAACCACCCCAACCAGACACACTACACACGCA^{GGGCCCGCGCGGGGCG}
CCCGCCCAAATCCCTAAGAGCACAAACACCAACACAACCACCCCAACCAGACACACTACACACGCA-3'

ssDNA#3

5'-GD2 aptamer/Dox loading linker#2/MYCN siRNA#2-3'

5'-CCGCCCAAATCCCTAAGAGCACAAACACCAACACAACCACCCCAACCAGACACACTACACACGCA^{GGGCCCGCGCGGGGCG}
CCCGGAGATGCTTGAGAA-3'

Supplementary Figure 2. Sequences and design of ANM.



ssDNA#1

5'-Control ssDNA/Dox loading linker#1/MYCN siRNA#1

5'-CCGCCCAAATCCCTAAGAGCGTAGATTCGATCGATCGGACTCGATCGCAGACACACTACACACGCA^{CCCGGGCGCGCGCCCGCGCCCGGGCGGAGTTGGTAAAGAATGA}-3'

ssDNA#2

5'-Control ssDNA/ Dox loading linker#2/Control ssDNA-3'

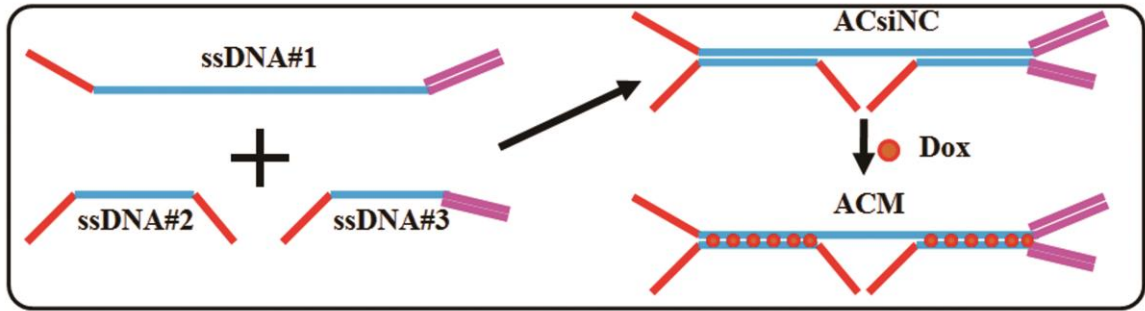
5'-CCGCCCAAATCCCTAAGAGCGTAGATTCGATCGATCGGACTCGATCGCAGACACACTACACACGCA^{GGGCCCGCGCGGGGCGCCCGCCCAAATCCCTAAGAGCGTAGATTCGATCGATCGGACTCGATCGCAGACACACTACACACGCA}-3'

ssDNA#3

5'- Control ssDNA /Dox loading linker#2/MYCN siRNA#2-3'

5'-CCGCCCAAATCCCTAAGAGCGTAGATTCGATCGATCGGACTCGATCGCAGACACACTACACACGCA^{GGGCCCGCGCGGGGCGCCCGGAGATGCTGCTTGAGAA}-3'

Supplementary Figure 3. Sequences and design of CNM.



ssDNA#1

5'-GD2 aptamer/Dox loading linker#1/Control siRNA#1

5'-CCGCCCAAATCCCTAAGAGCAGCAAAACACCAAACACAACCAACCCCAACCAGACACACTACACACGCA CCGGGCGCGCGCCCGC
GGCCCGGGCGCGCCCGCGGCUUCAGGAGCUGCCAGGUATT-3'

ssDNA#2

5'-GD2 aptamer/ Dox loading linker#2/GD2-aptamer-3'

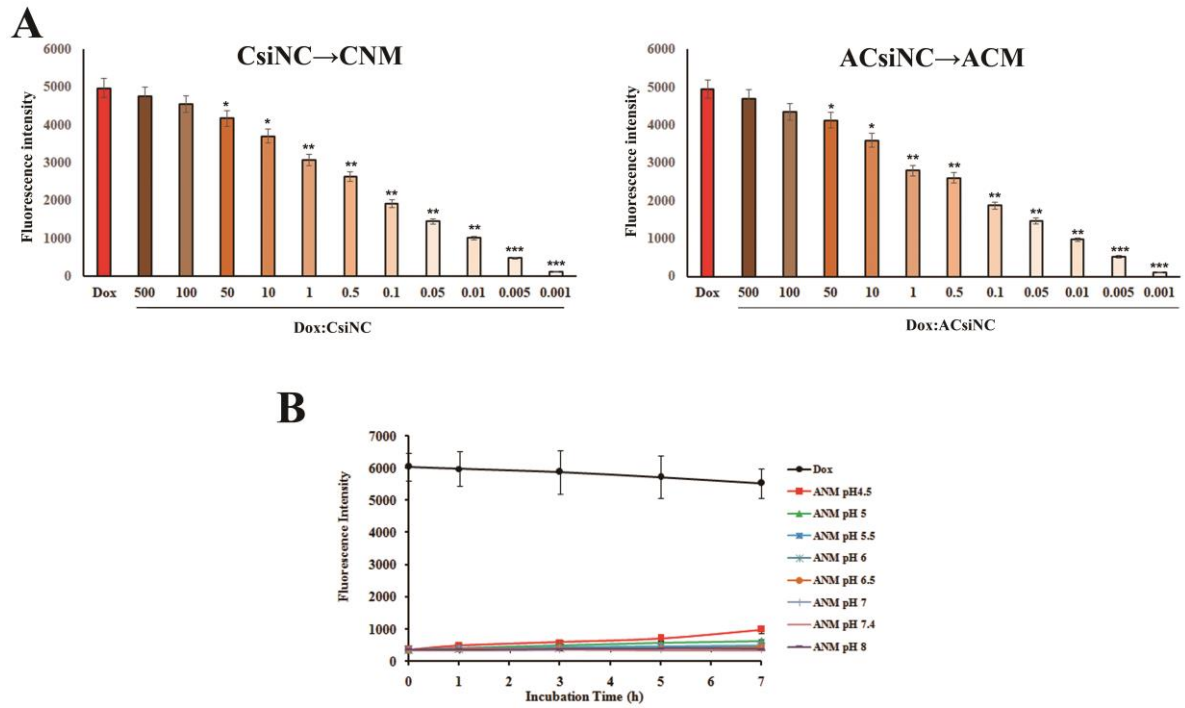
5'-CCGCCCAAATCCCTAAGAGCAGCAAAACACCAAACACAACCAACCCCAACCAGACACACTACACACGCA GGGCCCGCGCGGGCG
CCCCGCCCAAATCCCTAAGAGCAGCAAAACACCAAACACAACCAACCCCAACCAGACACACTACACACGCA-3'

ssDNA#3

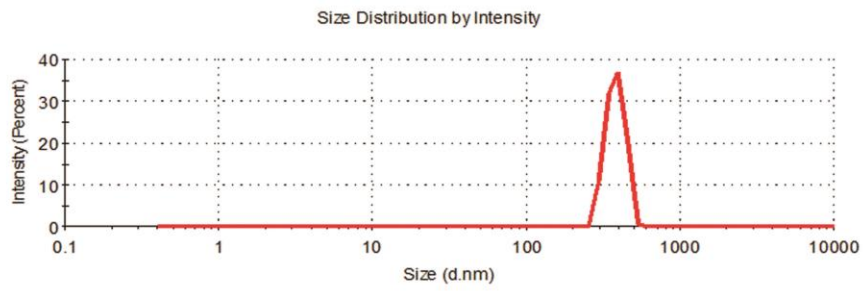
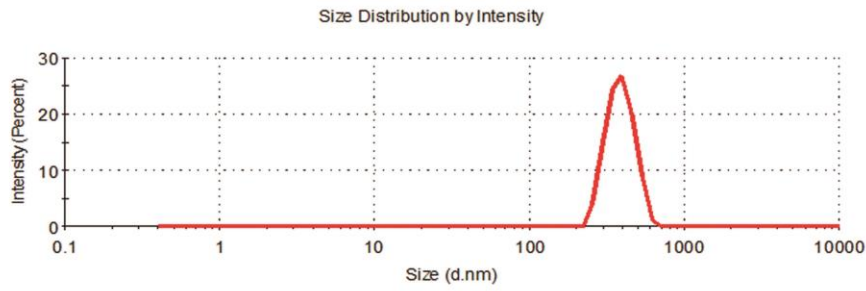
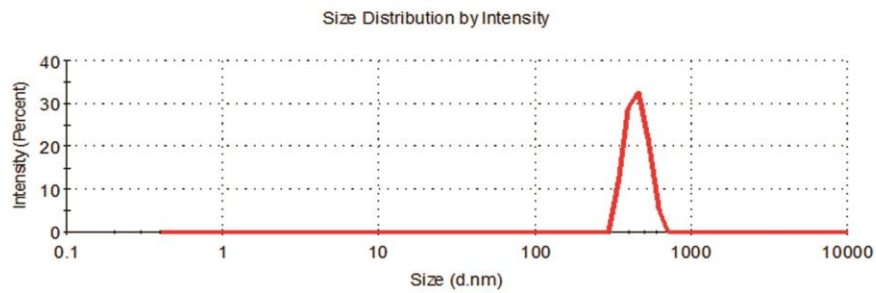
5'-GD2 aptamer/Dox loading linker#2//Control siRNA#2-3'

5'-CCGCCCAAATCCCTAAGAGCAGCAAAACACCAAACACAACCAACCCCAACCAGACACACTACACACGCA GGGCCCGCGCGGGCG
CCCUUCAGGAGCUGCCAGGUATT-3'

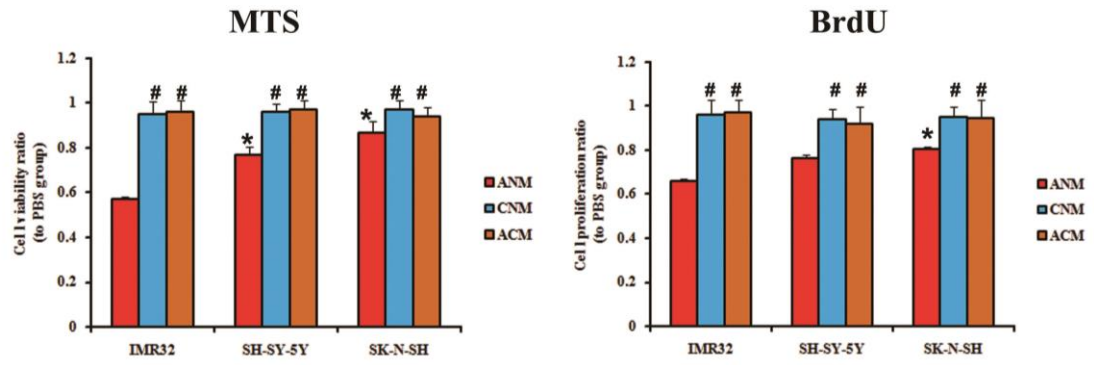
Supplementary Figure 4. Sequences and design of ACM.



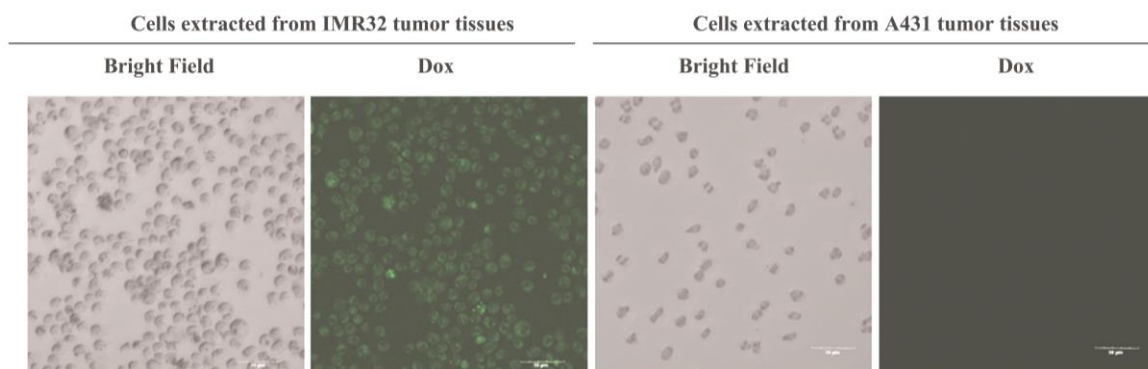
Supplementary Figure 5. Construction and stability. (A) Dox loading of ACsiNC and CsiNC. Fluorescence spectra of doxorubicin solution (5 nM) with increasing molar ratios of the ACsiNC and CsiNC. (B) Stability of ANM in different pH values. ANM was incubated at different pH buffers and fluorescence was assessed.

A**B****C**

Supplementary Figure 6. DLS analysis of ssDNA. (A) ssDNA#1; (B) ssDNA#2; (C) ssDNA#3.



Supplementary Figure 7. Cell viability and proliferation evaluated by MTS and BrdU ELISA assays. # indicating $p < 0.05$ compared with ANM group; * indicating $p < 0.05$ compared with the same conditions in IMR32.



Supplementary Figure 8. Visualization of Dox from extracted cells from IMR32 or A431 tumor tissue. After 1.5 h administration of ANM, mice were sacrificed and tumor tissues were isolated. Tumor tissues were chopped and digested by collagenase for 2 h at 37°C. Cells were washed by PBS and observed under confocal microscope (Scale Bar=30 μM).

Supplementary Table 1. Sequences of aptamers

Name	Sequences
	(5'-3')
Clone A	CCGCCCAAATCCCTAAGAGCACAAACACCAAACACAACCA
	CCCAACCAGACACACTACACACGCA
Clone B	CCGCCCAAATCCCTAAGAGACCCACCAACCACACACACACC
	CCAACCCAGACACACTACACACGCA