**Electronic Supplementary Information (ESI)**

# Extracellular pH-Manipulated In Situ Reconfiguration of Aptamer Functionalized DNA Monomer Enable Specifically Improved Affinity, Detection and Drug Delivery

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## Content list

**Table S1** All of the oligonucleotides used in this work.[1]

| Probe | Sequence (5'-3') |
|---|---|
| $Y_{1i}$ | CGA CCG ATG AAT AGC *T* ATC CGT ACC TAC TCG *TTTTT* **CCC CCC T CCC CCC** |
| $Y_{2i}$ | CGA GTC GTT CGC ACG *T* GCT ATT CAT CGG TCG *TTTTT* **CCC CCC T CCC CCC** |
| $Y_3$ | CGA GTA GGT ACG GAT *T* CGT GCG AAC GAC TCG GCT GTG AAC CAA GTC |
| Cy5-apt | Cy5-*T* GAC TTG GTT CAC AGC *TTT TTTT TTT* ACG CGC GCG CGC ATA GCG CGC TGA GCT GAA GAT CGT ACC GTG AGC GCG T |
| Cy5-con [2] | Cy5-*T* GAC TTG GTT CAC AGC *TTT TTTT TTT* ACT CAT AGT GTG TTT CAC ACT ATT TTA TCT TTG TTC TTA TCT TAT GAG T |
| $Y_{1c}$ [3] | CGA CCG ATG AAT AGC *T* ATC CGT ACC TAC TCG *TTTTT* TTT TTT T TTT TTT |
| $Y_{2c}$ [3] | CGA GTC GTT CGC ACG *T* GCT ATT CAT CGG TCG *TTTTT* TTT TTT T TTT TTT |
| $Y_{1cp}$ [4] | CGA CCG ATG AAT AGC TAT CCG TAC CTA CTC GTA GTC GAA TGT CTC GTT A |
| $Y_{2cp}$ [4] | CGA GTC GTT CGC ACG TGC TAT TCA TCG GTC GTA GTC GAA TGT CTC GTT A |
| $Y_{1cp'}$ [4] | CGA CCG ATG AAT AGC TAT CCG TAC CTA CTC GTT AAC GAG ACA TTC GAC T |
| $Y_{2cp'}$ [4] | CGA GTC GTT CGC ACG TGC TAT TCA TCG GTC GTT AAC GAG ACA TTC GAC T |

[1] In all sequences, split i-motif DNA sequences are in bold. The complementary ssDNA sequences used to replace split i-motif sequences are shown in blue. ZY11 sequence against SMMC-7721 cell is showed underlined, poly T in italic is used as linker for minimizing steric resistance.

[2] ConDM is assembled from Cy5-con, $Y_{1i}$, $Y_{2i}$, $Y_3$, which shows little affinity to target SMMC-7721 cells. [3] $AptDM_{Con}$ is assembled from Cy5-apt, $Y_{1c}$, $Y_{2c}$, and $Y_3$, which is incapable of crosslinking each other into bulk nanostructure in whatever pH. While, $ConDM_{Con}$ is assembled from Cy5-con, $Y_{1c}$, $Y_{2c}$, $Y_3$, which is neither affinitive to target cells nor sensitive to pH.

[4] AptDM-$C_1$ is assembled from Cy5-apt, $Y_{1cp}$, $Y_{2cp}$ and $Y_3$, while AptDM-$C_2$ is assembled from Cy5-apt, $Y_{1cp'}$, $Y_{2cp'}$, and $Y_3$. AptDM-$C_1$ and AptDM-$C_2$ can spontaneously crosslink each other into bulk nanostructure ($MDA_{cp}$) via sticky-end hybridization in whatever pH.

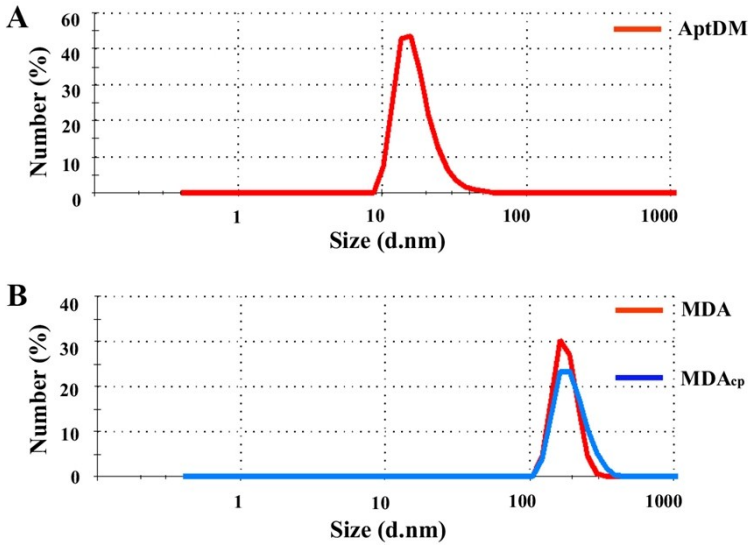


**Fig. S1** Dynamic light scattering analysis of the size of AptDM, MDA and $MDA_{cp}$, showing the mean diameters at 17.1, 178.5 and 195.2 nm, respectively.

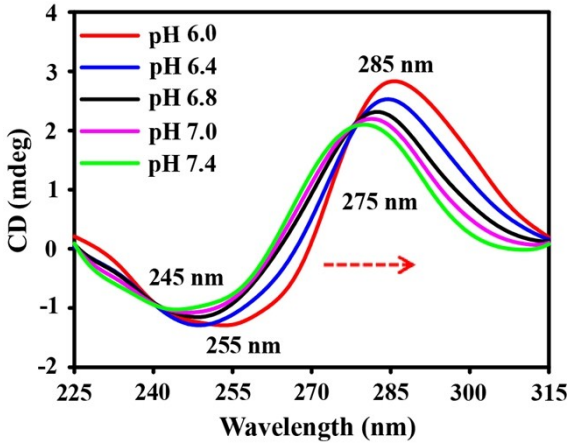


**Fig. S2** CD spectra of AptDM in PBS with different pH values. (Probe concentration: 1 μM.)

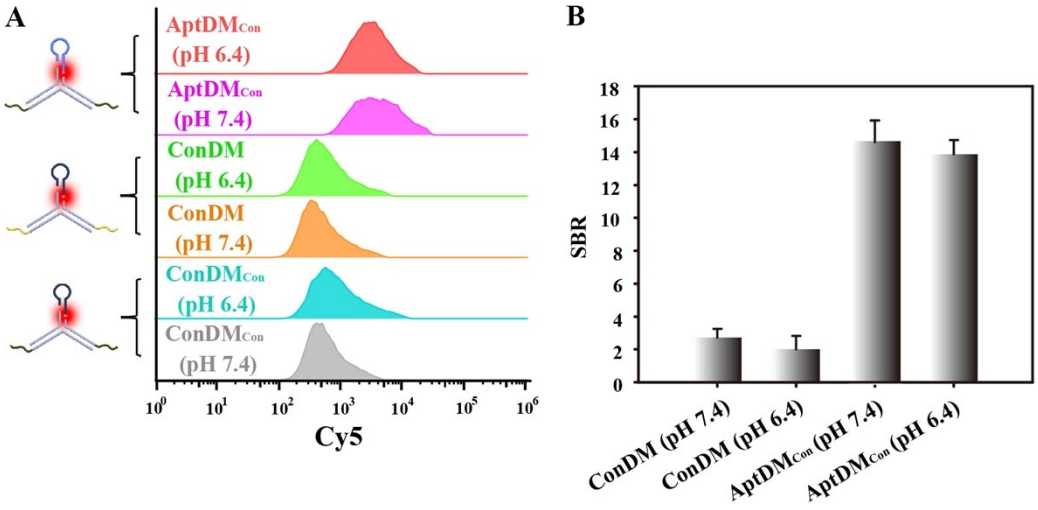


**Fig. S3** (A) Flow cytometric assays of SMMC-7721 cells after incubation with different probes in binding buffer with different pH values, respectively. (B) The corresponding signal-to-background ratio (SBR) of probes in (A) for detecting SMMC-7721 cells at different pH values. (Probe concentration: 50 nM.)

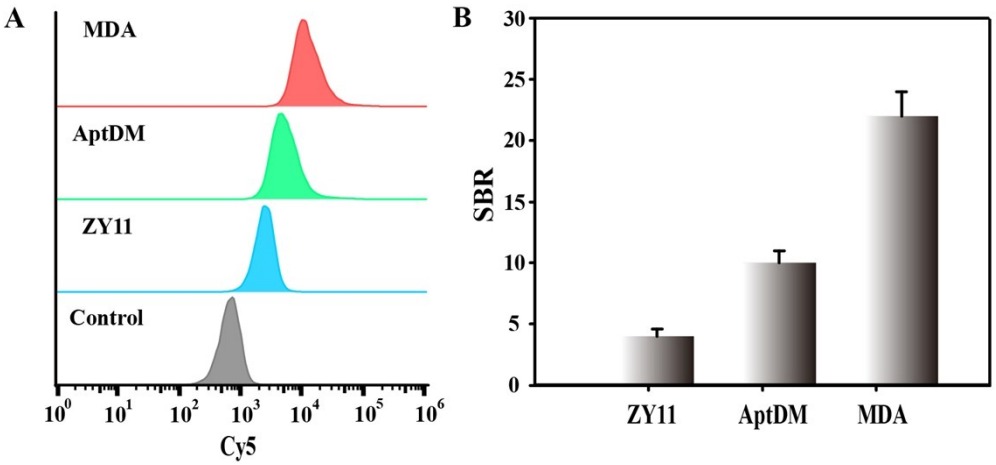


**Fig. S4** (A) Flow cytometric assay of binding ability of different probes to SMMC-7721 cells at 37 °C in binding buffer containing 0 mM $Mg^{2+}$. (B) The corresponding SBR of ZY11, AptDM and MDA probes in (A).

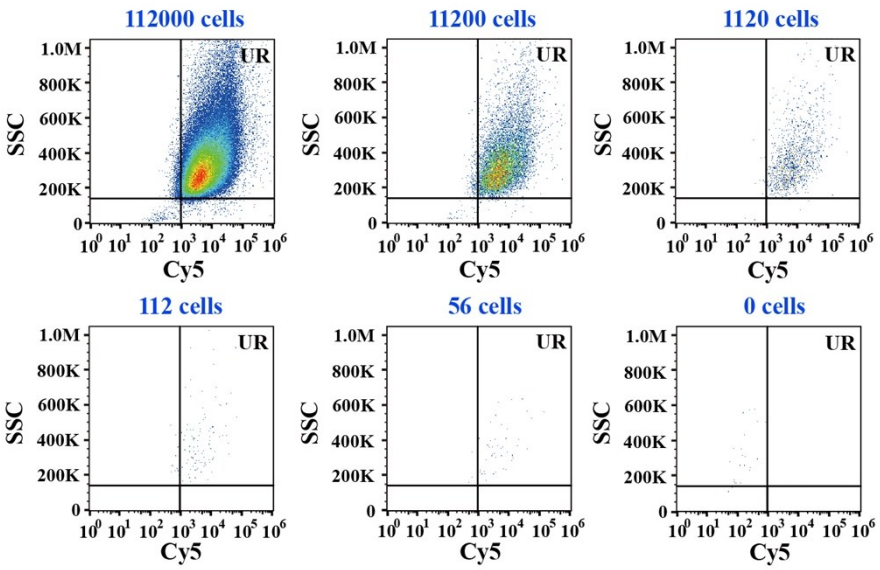


**Fig. S5** Flow cytometric assays of SMMC-7721 cells with decreasing cell number from $1.12 \times 10^5$ to 0 in 150 μL binding buffer after incubation with MDA.

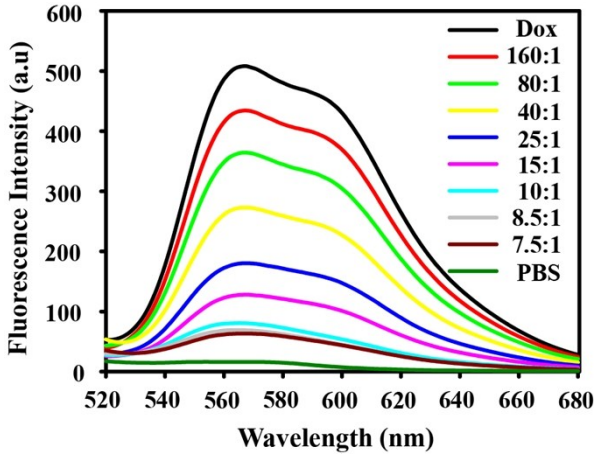


**Fig. S6** Fluorescence spectra of Dox solutions (1 μM) added with AptDM at various ratios of Dox to AptDM.