Electronic Supplementary Information (ESI)

Ag cluster-aptamer hybrid: specifically marking the nucleus of live cells

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S1:
The aptamer was synthesized and PAGE purified by TaKaRa Biotechnology (Dalian, China). The aptamer was used without further treatment. The sequence of the aptamer is as follows:
5'-CCCCCCCCATCTAACTGCTGCGCCGCCGGGAAAATACTGTACGGTTAGA
The sequence in red color is the short oligonucleotide attached to the sgc8c aptamer.

The procedure for the cluster synthesis was performed as follows: Msgc8 aptamer (18 μM) and $AgNO_3$ (1.125 mM) were separately dissolved in de-ionized water. Subsequently $NaBH_4$ (1.125 mM) was introduced into the solution to reduce $AgNO_3$ under vigorous stirring for 10 hours, and the products were purified by dialysis (Merck, Midi D-tube membrane, molecular weight cut off: 10,000 Da).

S2:
Spectra study of the cluster-aptamer:
The cluster solution was directly used for absorption spectra study. Absorption spectra were obtained on UV-1800 (Shimadzu) with Milli-Q water as the reference solution.

Fluorescent spectra were monitored on a RF-5301 (Shimadzu) (slit width: 10 nm). Due to the strong fluorescence of the cluster, an 11 times diluted solution was used when excited at 517 nm, however, the spectra obtained at 403 nm excitation was without dilution. The strong contrast between the intensity of the fluorescence supported the idea that Ag_3 was the cluster in the solution with the stronger fluorescence and was better suited for the cell-imaging.

The FT-IR spectrum was recorded with sample powders on a Nicolet 750 FT-IR spectrometer at 4 cm^{-1} resolution. Cluster solution (1 mL) was centrifuged at 6000 rpm for 2 hours and concentrated to 40 μl for drying on a glass slide at room temperature. The powders were scraped and pressed tightly on diamond windows for the FT-IR observations.

Mass spectra were obtained on a MALDI-TOF-MS (Bruker Daltonics Autoflex) with a 3-HPA matrix in linear mode. Cluster solution (2 ml) was concentrated to 30 μl for the analysis.

S3:
Circular dichroism spectra were measured on a Jasco J-715 spectropolarimeter at room temperature (cell length: 1 mm; resolution: 0.01 mdeg; scanning speed: 200 nm/min; accumulation times: 3).

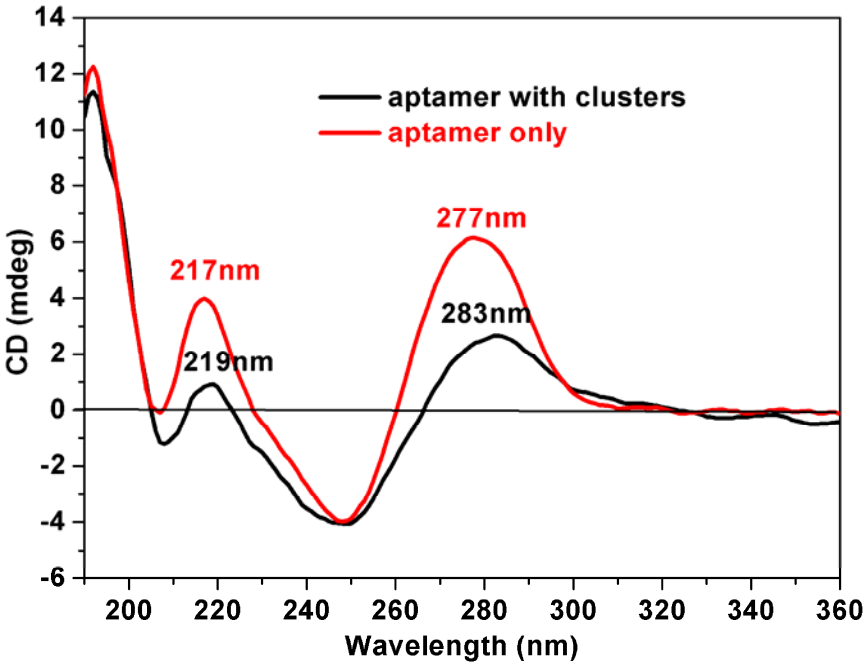

Figure S1. Circular dichroism of the cluster-aptamer solution.

S4:
Methods for the cell assay:

The CCRF-CEM cells were cultured in RPMI-1640 medium, concentrated cluster solution was added to the medium with a final concentration of 0.19 mM. The cells were cultured for 2 hours at 20°C for nucleus staining, then 1.2 μL Hoechst 33342 (1 mg/ml) was added to the medium to stain the cell nucleus. A volume of 120 μl of cells (cell density: 1.15×10^{8}/ml) were washed with PBS buffer (200 μl) three times to remove the free cluster-aptamer and the free Hoechst 33342. After resuspension in 80 μl PBS buffer, the cells were dropped on a slide with a coverglass for observation by confocal fluorescence microscopy.

Images were obtained on a spinning disc cofocal microscope equiped with a Nikon TI-E inverted microscope with a 60× oil immersion lens (Perkin Elmer).

S5:
Methods for the cell-specific experiment:
Hela cells were seeded in the cell culture dish at 2700 cell/well, after incubated at 37℃ overnight, the cluster-aptamer hybrid was introduced at a final concentration of 0.19mM. The cells were continued incubated at room temperature for another two hours. Then the cells were washed with PBS buffer for 2 times, and the cell culture dish was mounted on the microscopy for observation.
Contrast the two images of the cells, the Hela cells cultured with cluster-aptamer hybrid showed no fluorescence from the cluster, which well testified the specificity of the hybrid.

The results were as follows:

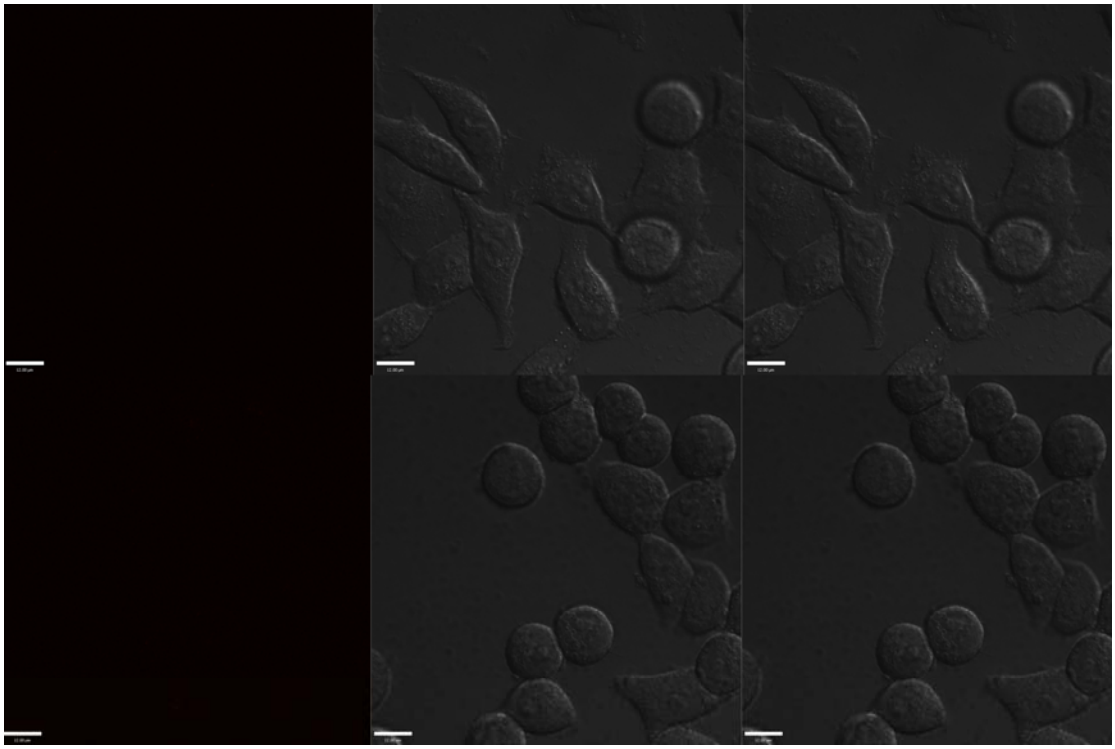

Figure S2. Confocal microscopy images of the Hela cells incubated with cluster-aptamer hybrid. The upper pannel is the control cells cultured in the DMEM medium without cluster-aptamer hybrid, the lower panel is the cells incubated with cluster-aptamer hybrid. The right panel is the image excited with 561 nm, the middle panel is the bright field image, and the left panel is the merged image of the right two channels.

S6:

The cell viability was tested with trypan blue exclusion assay. CCRF-CEM cells were seeded in a 96-well plate at the density of 5.3×10^5/cell. The cluster-aptamer hybrid was introduced at the concentraton of 0.19mM. After cultured for different time, 25uL 0.4% trypan blue was introduced. After 1 minutes, 9uL of the cellls were dropped onto the hemocytometer to count the cells.

The data showed that at the same concentration with the Ag cluster-aptamer hybrid used for nucleus imaging, Msgc8 aptamer showed no cytotoxicity towards cells, hence the toxity must came from the silver clusters.

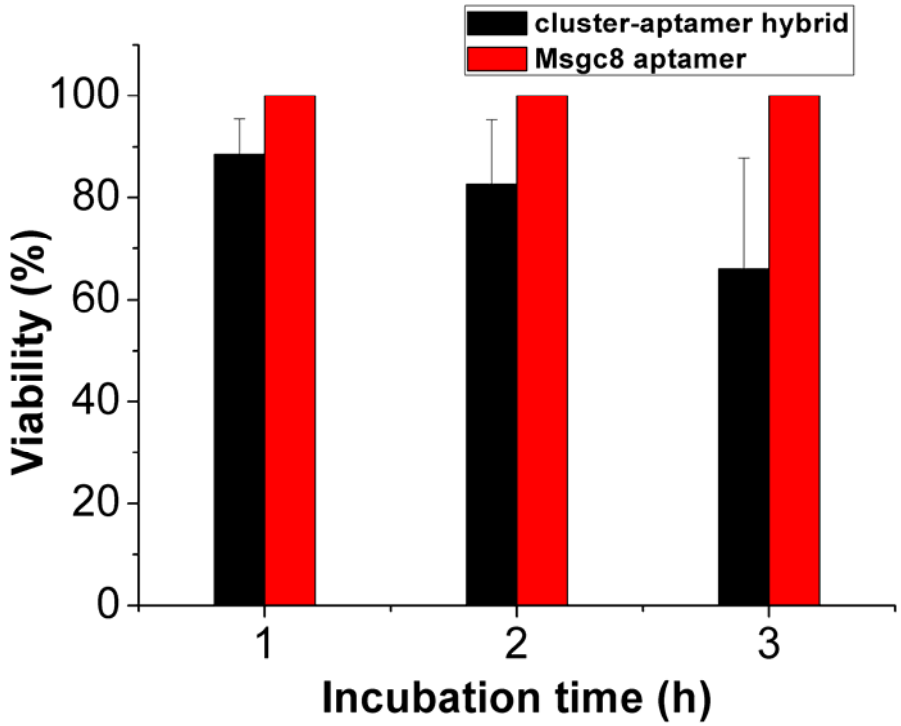

Figure S3. Trypan blue exclusion assay. The cells were incubated with 0.19mM cluster-aptamer hybrid for 1, 2 and 3 hours, respectively.