Supporting Information

Synthesis of Fluorescent Dye-doped Silica Nanoparticles for Target-Cell-Specific Delivery and Intracellular MicroRNA Imaging

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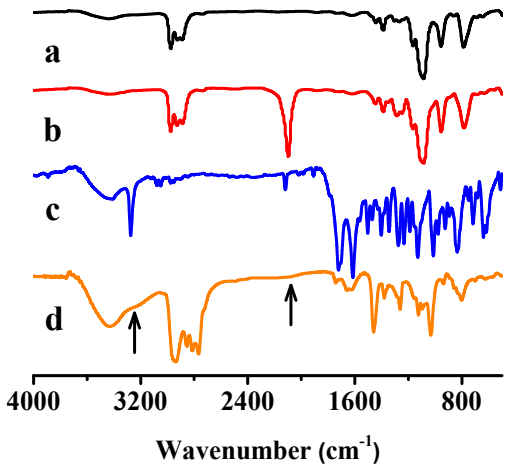

Figure S1. FT-IR spectra of a) 3-Chloropropyltriethoxysilane, b) 3-Azidopropyltriethoxysilane, c) 7-Propinyloxy coumarin, d) Coumarin-functionalized siloxane.

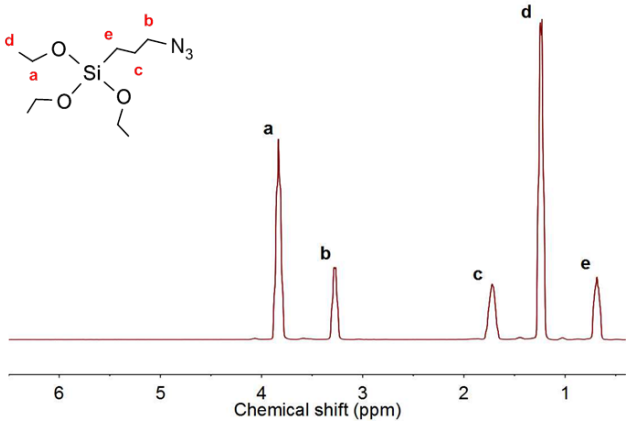

Figure S2. [1]H-NMR spectra of 3-azidopropyltriethoxysilane.

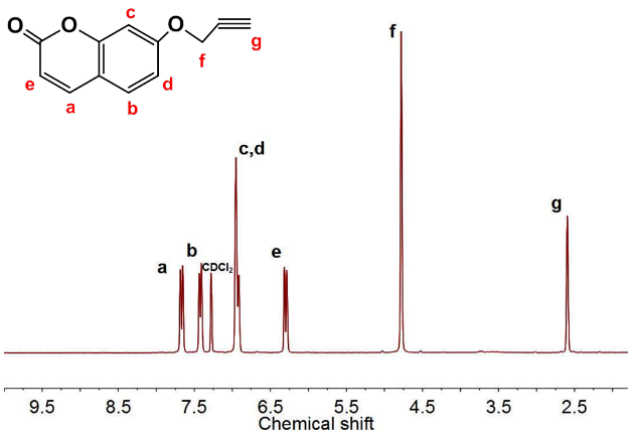

Figure S3. ^{1}H-NMR spectra of 7-propinyloxy coumarin.

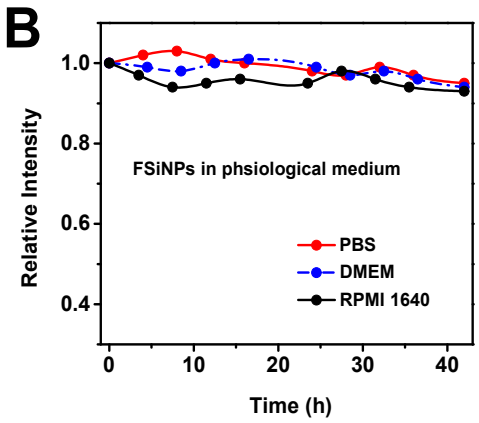

Figure S4. Colloidal stability characterized by the fluorescence fluctuation of FSiNPs suspended in different types of buffers.

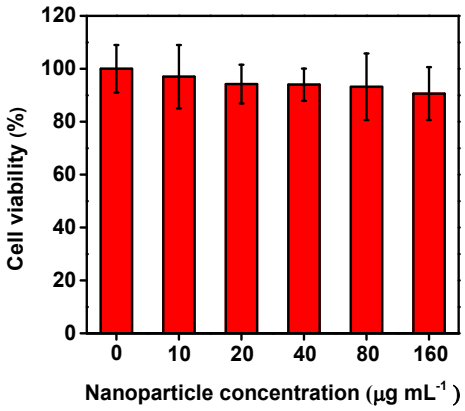

Figure S5. Cytotoxicity induced by FSiNPs in MCF-7 cells.

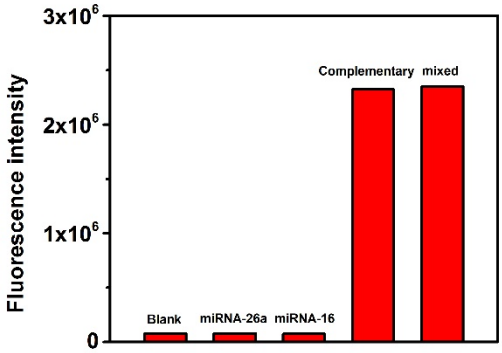

Figure S6. Selectivity of the gene probe to miRNA-21 by comparing it to the interfering miRNA and the mixed sample.

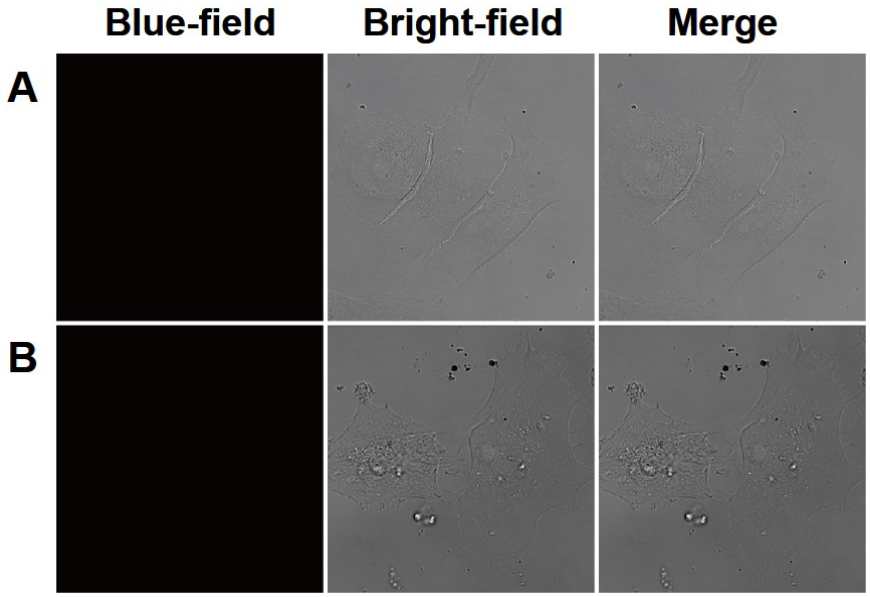

Figure S7. Confocal blue-field, bright-field and overlay images of MCF-7 cells and MCF-10A. MCF-7 treated with FSiNPs (A, 100 μg mL^{-1}), and FSiNPs-MB (B, 100 μg mL^{-1}), respectively. MCF-10A treated with FSiNPs-AS (C, 100 μg mL^{-1}) at 37 ºC for 3 h.

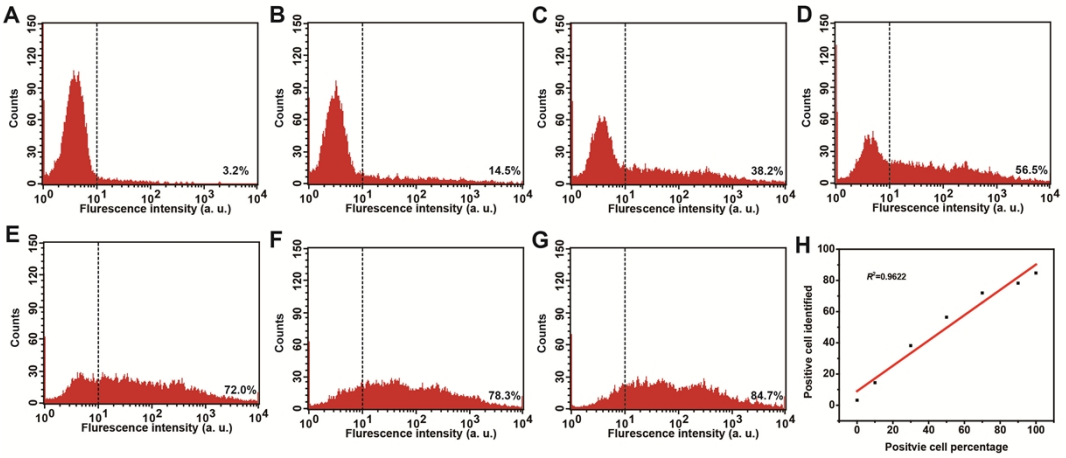

Figure S8. Selective recognition of MCF-7 cells in mixed cell with FSiNPs-AS. Quantification of cell uptake for FSiNPs-AS. Flow-cytometric analysis of cell mixture sample containing different percentages of MCF-7 cells (A-G: 0%, 10%, 30%, 50%, 70%, 90%, and 100%, respectively). (H) Comparison of the percentage of positive cells (MCF-7) input and the percentage of positive cells identified by the FSiNPs-AS from each cell sample.

Quantum yield. The quantum yield of FSiNPs was calculated with equation:

$$Q = Q_R\left(\frac{I}{I_R}\right)\left(\frac{A_R}{A}\right)\left(\frac{\eta^2}{\eta_R^2}\right)$$

Where Q is the quantum yield, I is the integrated emission peak areas, and A is the absorbance. The subscript R refers to the reference fluorophore of known quantum yield. Here Quinine sulfate was used as reference, which has a quantum yield of 54.6% when dissolved in 1N H_2SO_4. 1N H_2SO_4 had a refractive index η_R of 1.346, whereas the refractive index η of water was 1.33.

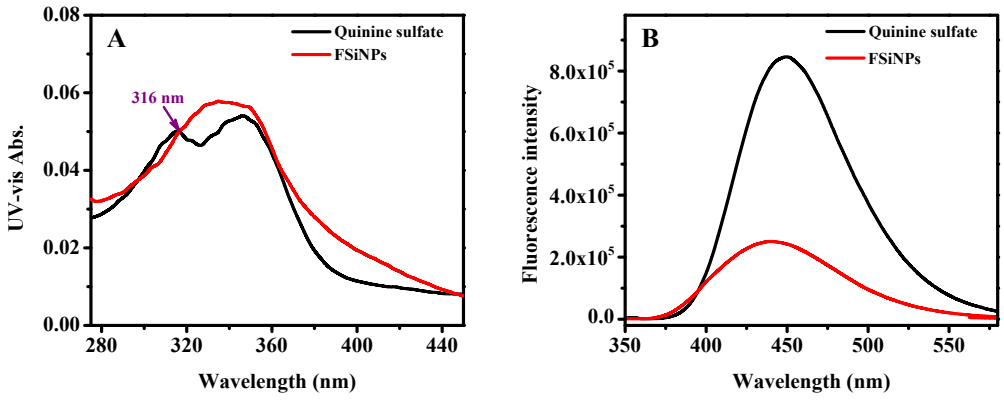

Figure S9 (A) Absorbance spectra and (B) fluorescence emission spectra of the standard Quinine sulfate and FSiNPs with excitation at 316 nm, where the absorbance values of them are equal.

The MTT assay of FSiNPs-AS/MB showed that the cell viability was maintained > 90% even at the FSiNPs-AS/MB dosage level, up to 160 μg mL^{-1}, which indicated low cytotoxicity of FSiNPs-AS/MB (Figure S8).

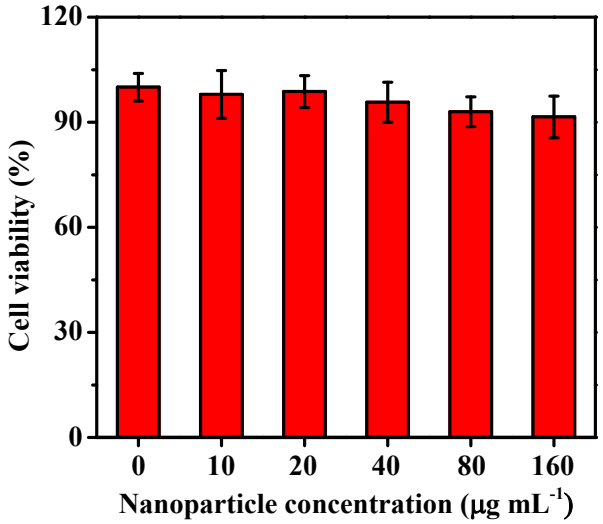

Figure S10. Cytotoxicity induced by FSiNPs-AS/MB in MCF-7 cells.

To verify that the disulfide linkage was indeed cleaved in reductive condition, the nanoprobes were incubated in a buffer solution containing glutathione (GSH) and dithiothreitol (DTT) for 2 h at 37 ºC, and the mixture was then separated with 1% Agarose gel in 1 × DNA loading buffer (DLB). Electrophoresis was carried out at 200 V for 15 min in buffer. The resulting migration pattern was revealed under UV irradiation. The nanoprobes in the GSH (band 2) or reduced by DTT (band 3) exhibited the same migration pattern as the gene probe (band 1), which indicated that the disulfide linkage was successful cleavage between nanoparticles and gene probe in the reductive environment. Band 4 is the nanoprobes in PBS (pH 7.2), the little migration resulted from the big size of the nanoparticles, which indicated that the gene probe conjugated on the nanoparticles was not damaged in the neutral environment (Figure S9).

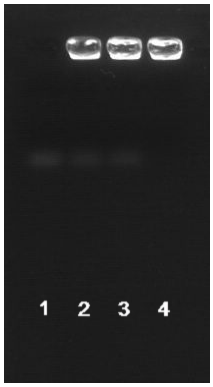

Figure S11. Electrophoresis images of nanoprobes in different conditions.

We evaluated the inernalisation efficiency of nanoprobes with spectrofluorometry [1]. The cells were seeded onto a 12-well-plate (200 000 cells/well) and the cells were grown for 12 h at 37 ºC. After the cells were washed with HEPES-buffered Krebs-Ringer solution (HKR) for three time, 1 mL fresh DMEM containing 100 μg mL^{-1} FSiNPs-AS was dropped and incubated at 37 ºC for 3 h. The cells were then washed three times with PBS, and the resulting cells were harvested. Cells were lysed with 0.1% Triton X-100 in HKR (15 min, 0 ºC), and analyzed with spectrofluorometer. The inernalisation efficiency (%) was calculated by $(I_{test}/I_{total}) \times 100\%$, where I_{test} is the fluorescence intensity of test, I_{total} is the fluorescence intensity of added total amount nanoparticles. The internalisatin efficiency was ca. 64.5%.

[1] M. Mäe, H. Myberg, Y. Jiang, H. Paves, A. Valkna, U. Langel, Biochim, Biophys. Acta, 2005, 1669, 101.