Supporting Information

Versatile FRET-Based Mesoporous Silica Nanoparticles for Real-Time Monitoring of Drug Release

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MATERIALS

N-Boc-cysteine, 2,2'-dithiodipyridine, 1-adamantanethiol, 7-hydroxycoumarin-3-carboxylic acid, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl), *N*-hydroxysuccinimide, triethoxysilane (TEOS), (3-aminopropyl)triethoxysilane (APTES), *β*-cyclodextrine (β-CD), fluorescein isothiocyanate (FITC), 4-dimethylaminopyridine (DMAP) were purchased from Sigma-Aldrich or TCI Chemical and used as received.

METHODS

UV-vis absorption spectra were recorded on a Varian Cary 50 spectrophotometer. Fluorescence spectra were recorder on a Varian Cary Eclipse fluorescence spectrophotometer. FT-IR spectra were collected on an Avatar Nicolet FT-IR330 spectrometer. Raman spectrum characterizations were performed on Laser Raman, Renishaw inVia Raman microscope. ^{1}H NMR was acquired on Varian 400MHz NMR spectrometer. ESI-MS was collected on Finnigan LCQ^{TM} DUO LC/MS spectrometer. Transmission electron microscopy (TEM) was performed on a Topcon 002B electron microscope at 200 kV. Sample preparation was carried out by placing a drop of the freshly prepared colloidal solution on a carbon-coated copper grid and allowing the solution to evaporate. Nitrogen adsorption-desorption measurements were performed on a Micromeritics Tristar-3000 surface area analyzer at –196°C. The sample was dried at 200°C for 3 h before analysis. The Burnauer-Emmett-Teller (BET) specific surface areas were calculated using the first 10 experimental data points. Pore volumes were determined from the amount of N_2 adsorbed at the single point $P/P_0 = 0.98$.

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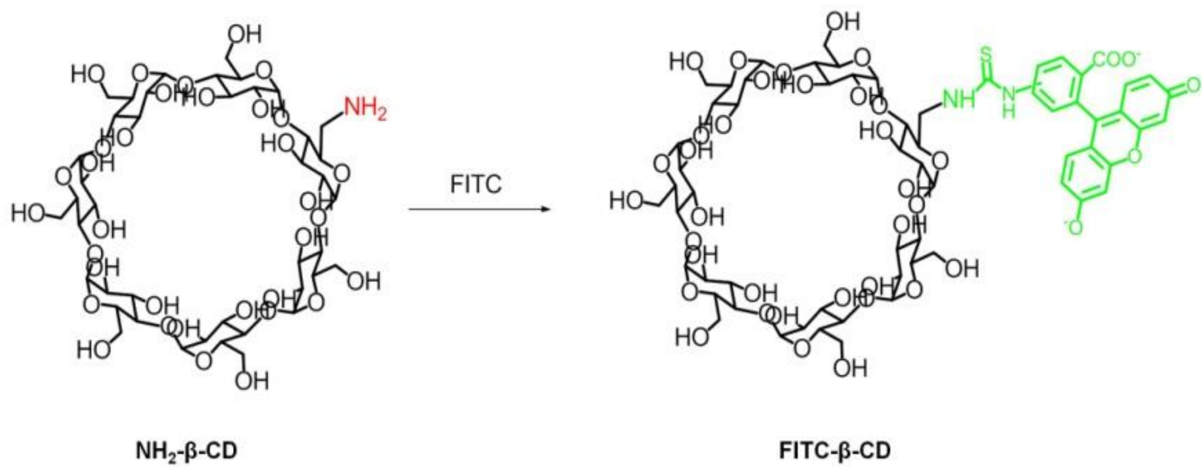


Figure S1. Schematic illustration depicting the synthesis of FITC-β-CD

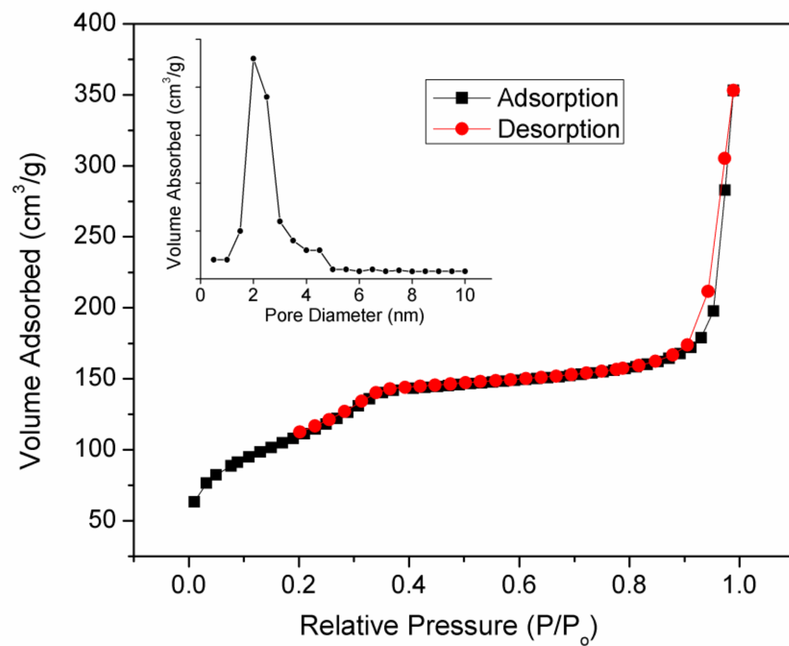


Figure S2. N_2 adsorption-desorption isotherms of the prepared CHC-MSNs. The inset figure shows the pore diameter distribution of the CHC-MSNs

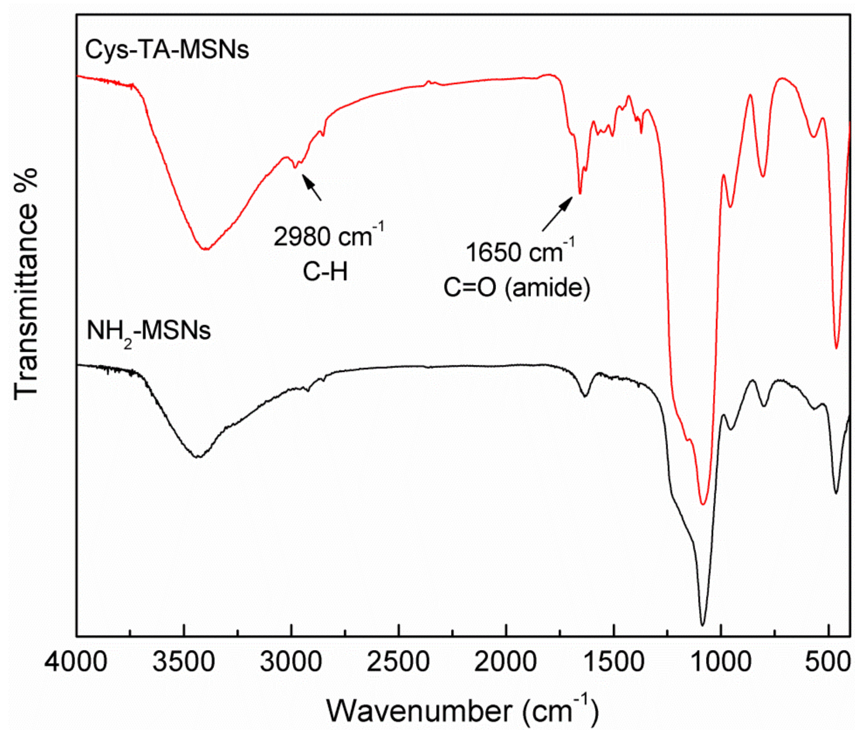


Figure S3. FT-IR spectrum of the as prepared MSNs.

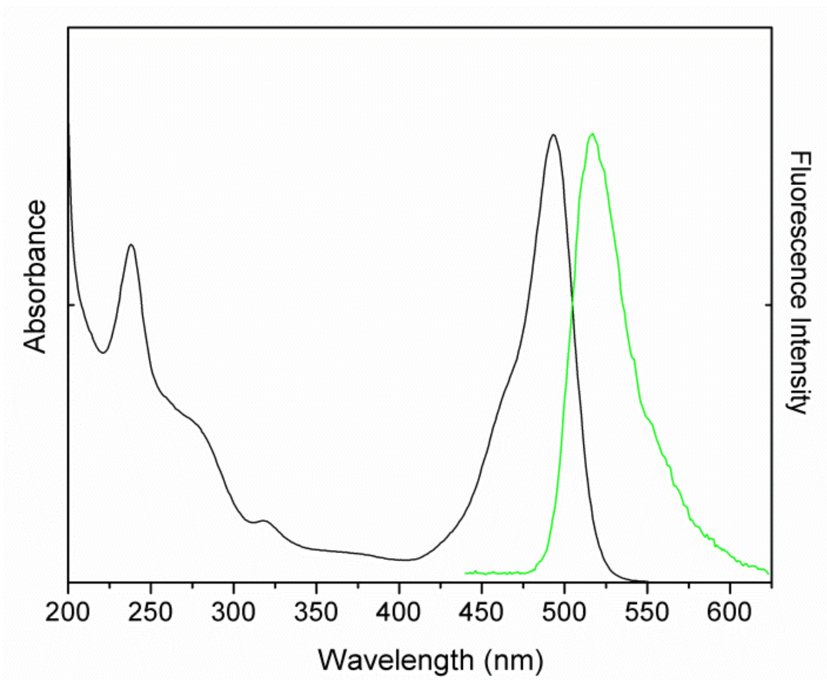


Figure S4. UV-Vis absorption and fluorescence spectrum of FITC-β-CD.

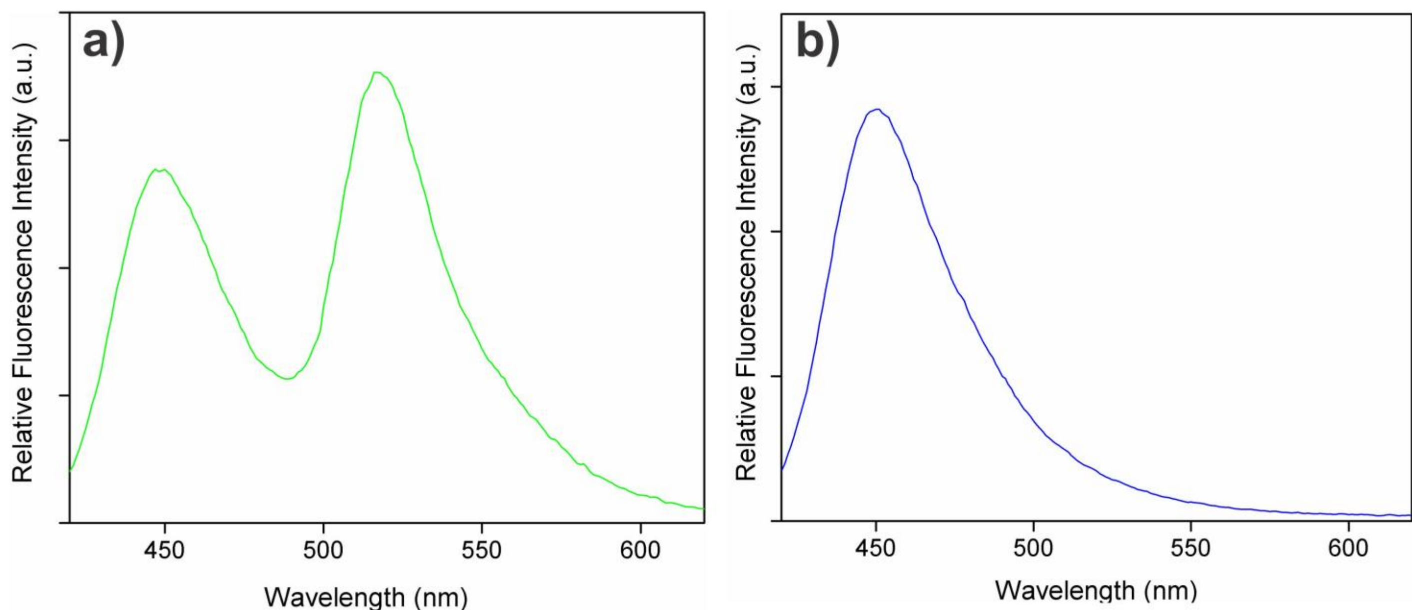


Figure S5. Emission profiles of FRET-MSNs. (a) Dual emission peaks corresponding to both coumarin (450 nm) and FITC (520 nm) emission when the FRET-MSNs are excited using coumarin's excitation wavelength (*i.e* 405 nm). This result confirms the presence of an intact FRET donor-acceptor pair on the surface of FRET-MSNs in the absence of any reducing stimuli. (b) A single emission peak corresponding to coumarin (450 nm) is seen when the FRET-MSNs are treated with gutathione (GSH, 5 mM) for 10 mins and then excited using coumarin's excitation wavelength (*i.e.* 405 nm).

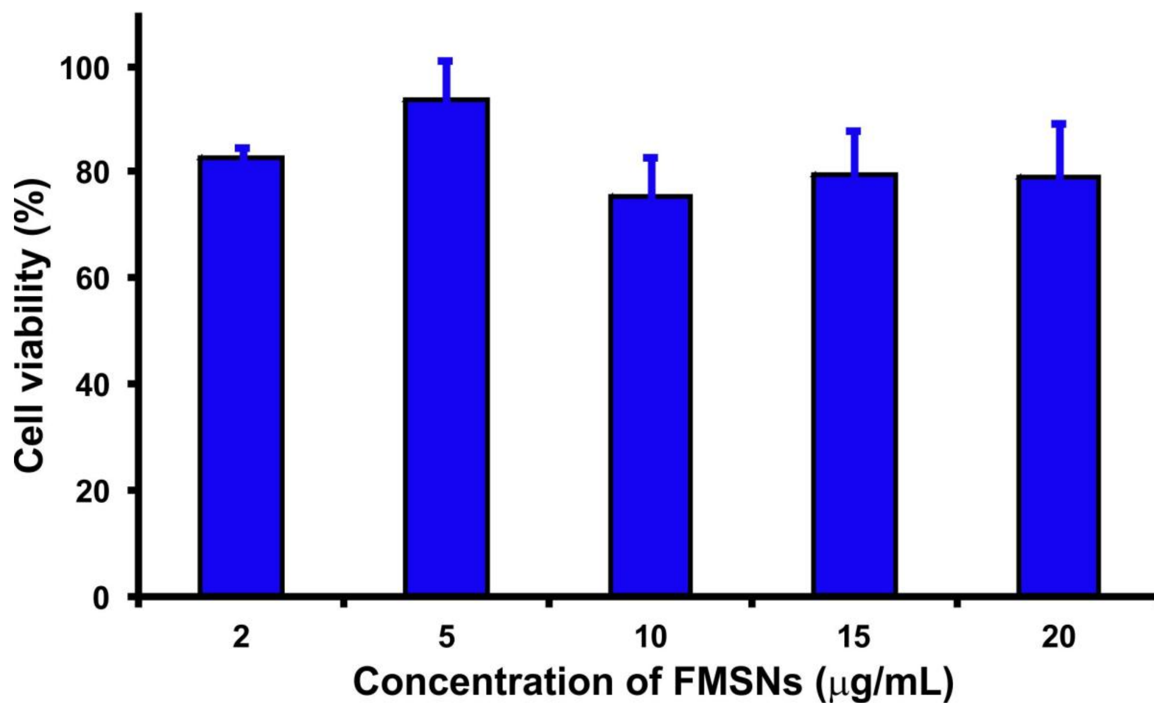
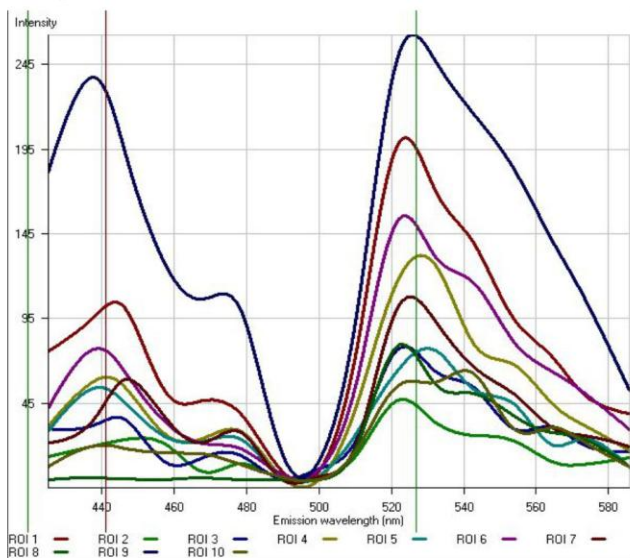
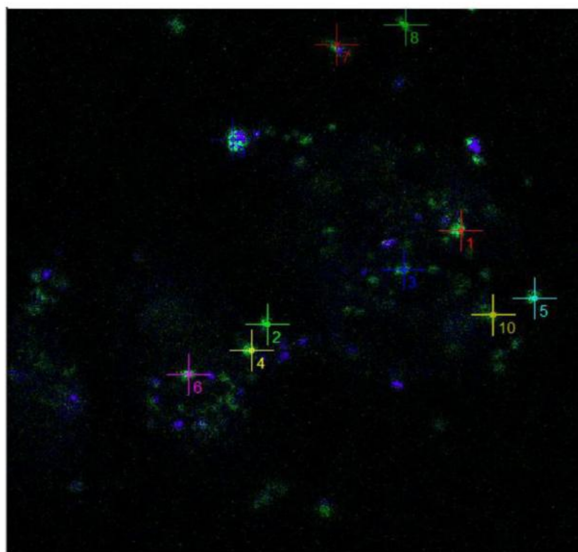


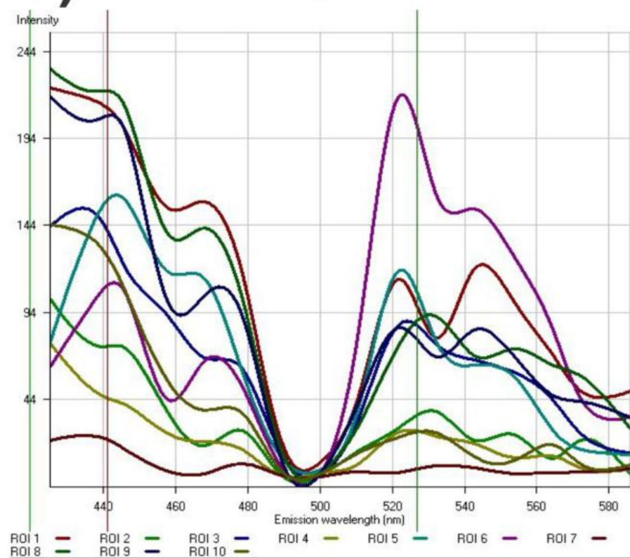
Figure S6. Percent cell viability of HeLa cells following treatment with increasing concentrations of FRET-MSNs. The cell viability was analyzed 48 h after treatment with FRET-MSNs using CellTiter 96® AQueous One Solution Cell Proliferation Assay (MTS). All experiments were done in triplicates and the average and standard deviation for each condition are represented.

a) FRET ON





b) FRET OFF



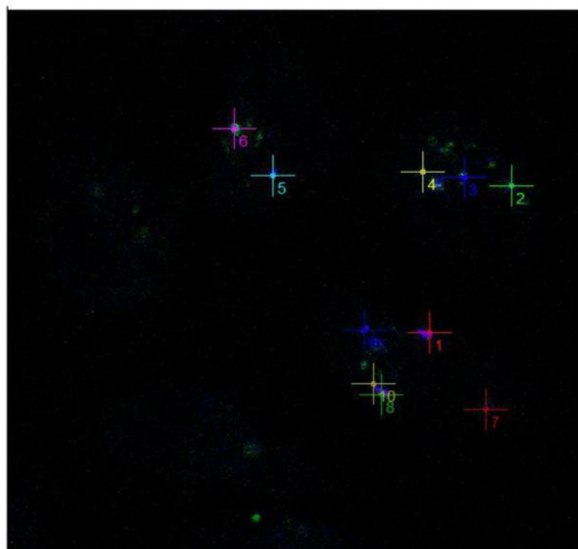


Figure S7. Confocal images depicting the selected data points used for generating the emission profiles shown in Figure 5A (in the main manuscript)

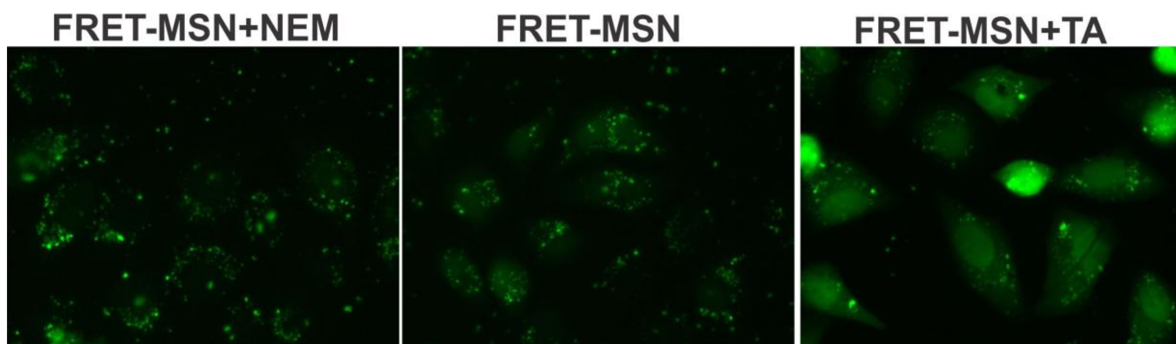


Figure S8. Fluorescence microscopy images showing the change in the fluorescence intensity (FITC) when the HeLa cells were treated with FRET-MSNs after varying intracellular GSH concentration. For this purpose, the HeLa cells were treated with *N*-ethyl maleimide (NEM, a GSH scavenger, 5 μM) and thioctic acid (TA, a GSH synthesis enhancer, 10 μM), 10 min prior to adding FRET-MSNs.

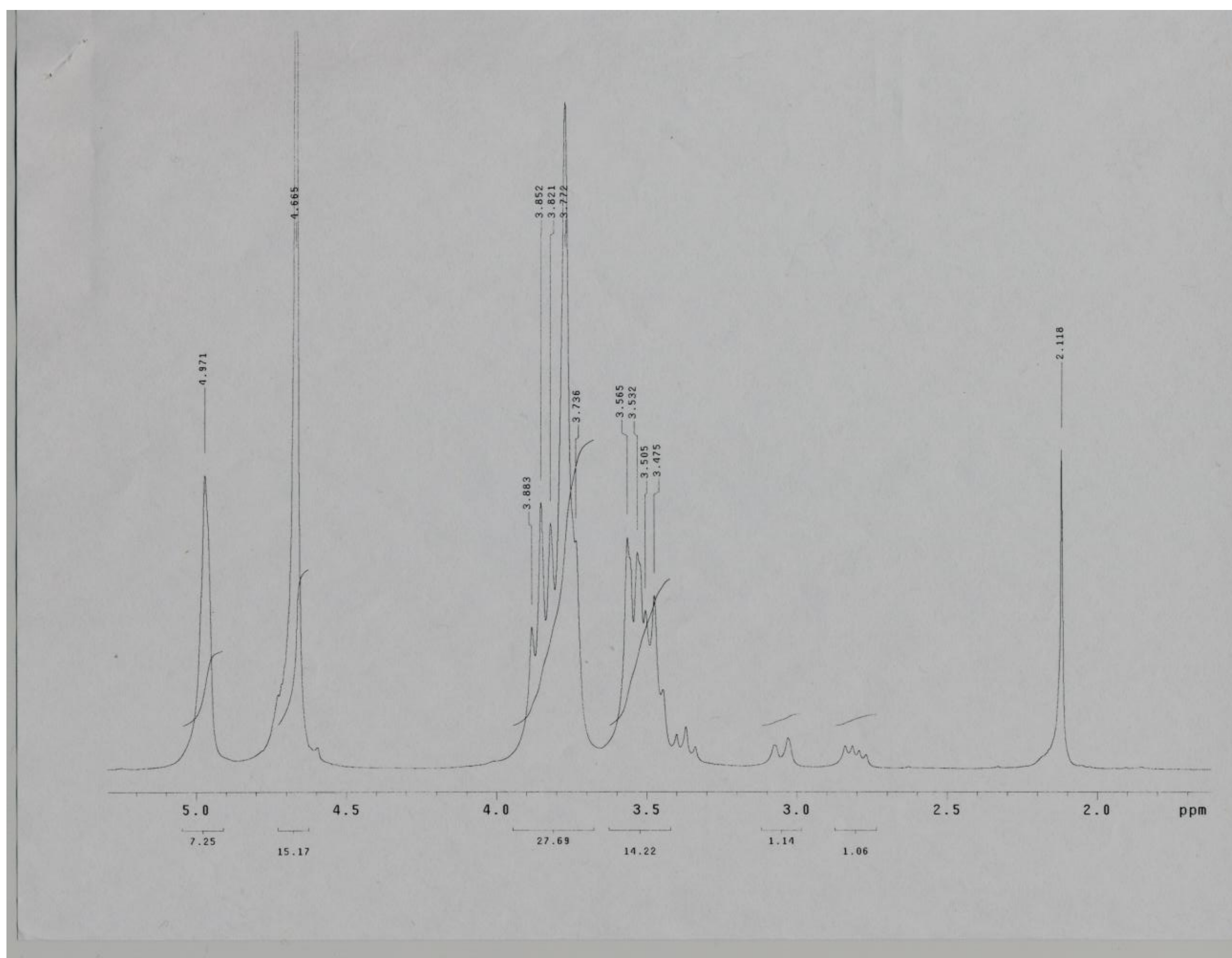


Figure S9. ^{1}H NMR spectrum of NH_2-β-CD (D_2O, 300 MHz).

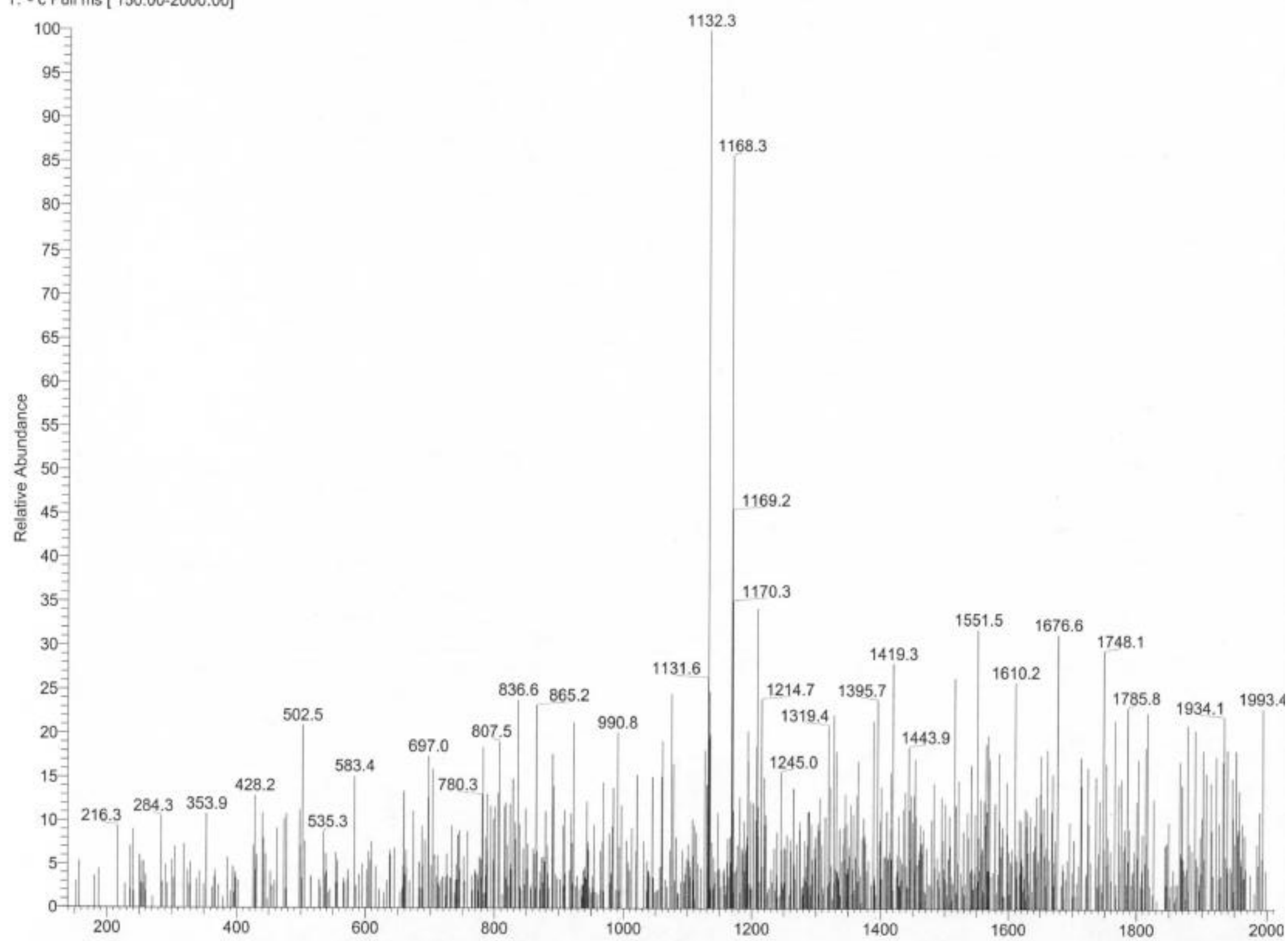


Figure S10. ESI-MS spectrum of NH_2-β-CD.

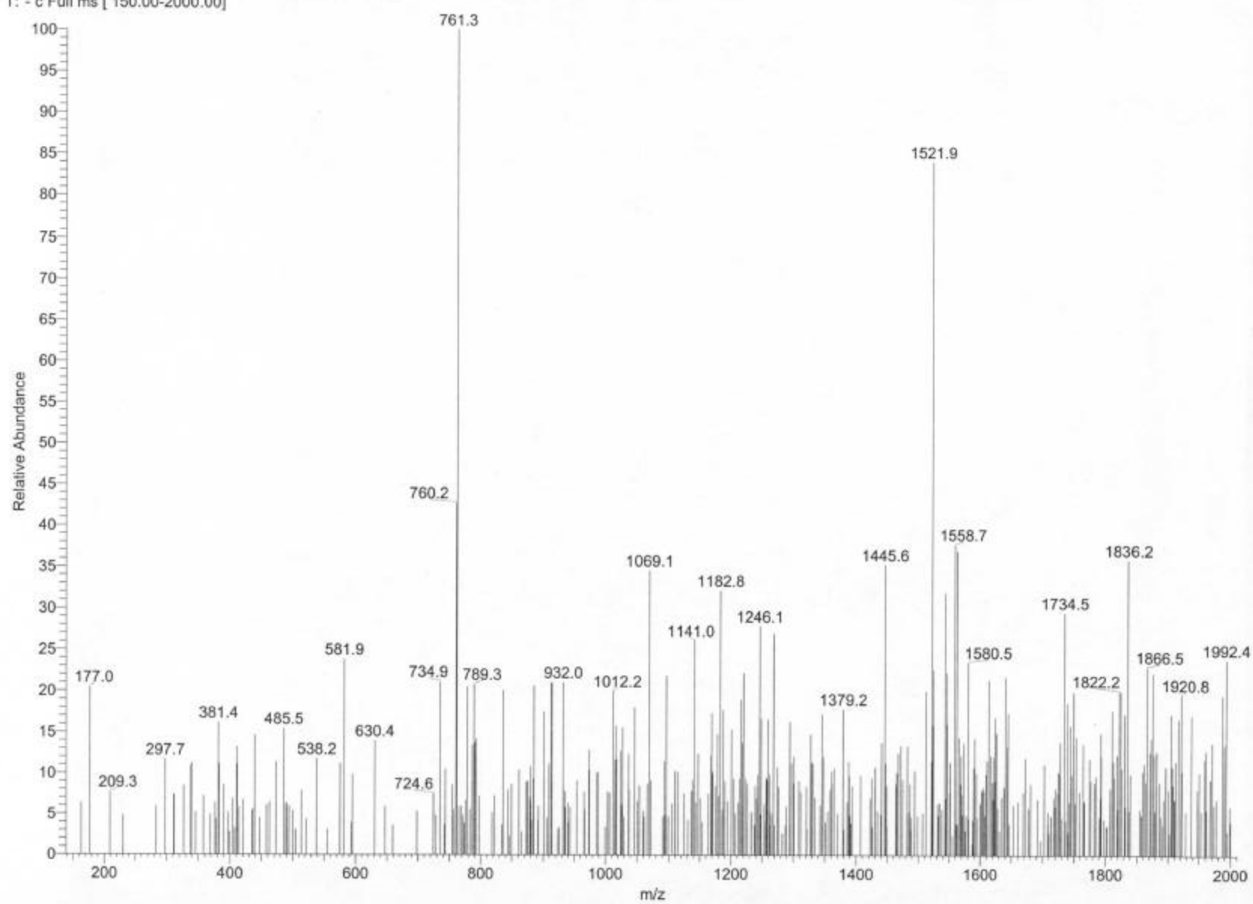


Figure S11. ESI-MS spectrum of FITC-β-CD.