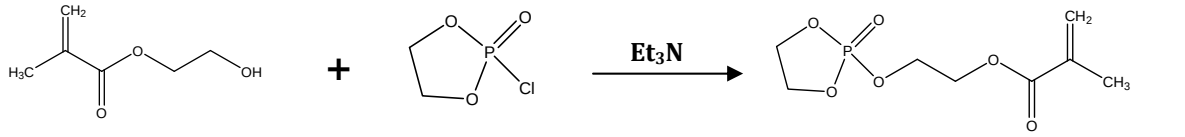
Supporting Information

Preparation and Characterization of MRI-active Gadolinium Nanocomposite Particles for Neutron Capture Therapy

by Heui Kyoung Cho et al.

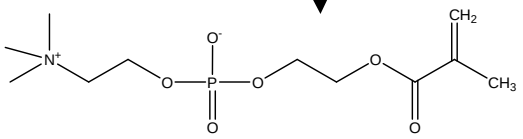
1. Synthesis and characterization of MPC monomer

1st step



2-hydroxyethyl methacrylate (HEMA) | **Ethylene chlorophosphate (COP)** | **HEMA-COP**

2nd step **Me_3N**



MPC

Scheme S1 Synthesis of 2-methacryloyloxyethyl phosphorylcholine from HEMA and COP.

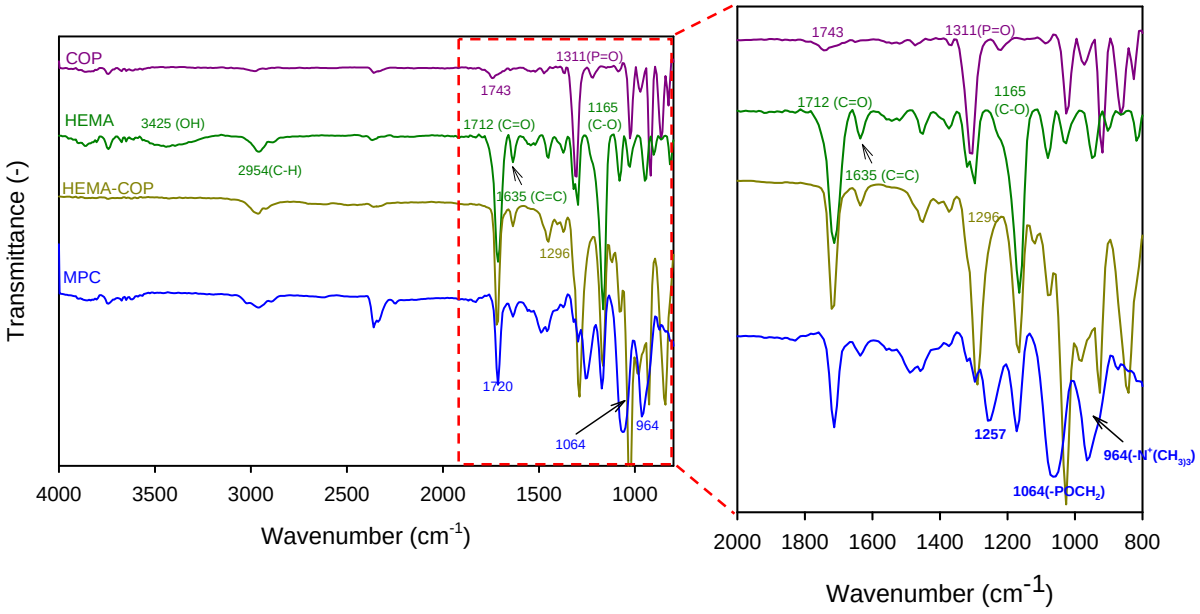
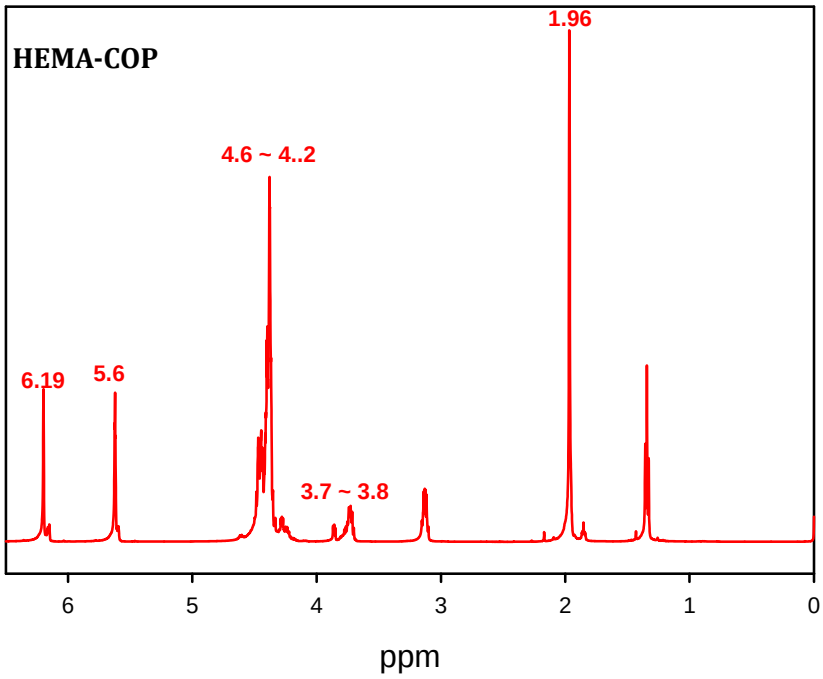


Figure S1. FT-IR spectra of COP, HEMA, HEMA-COP and MPC.



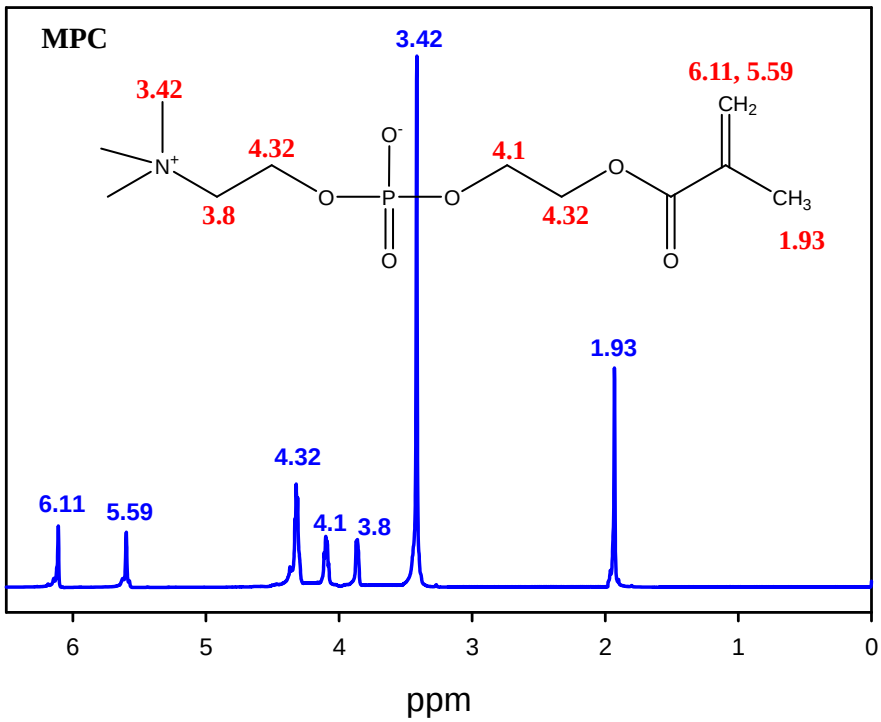


Figure S2. FT-IR ^{1}H NMR of HEMA-COP and MPC.

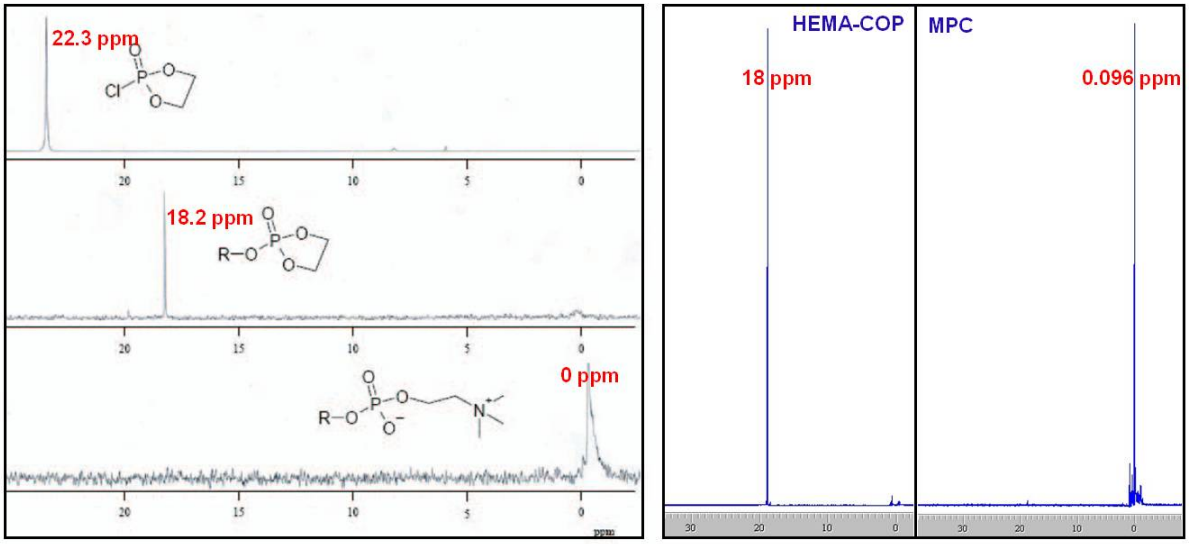
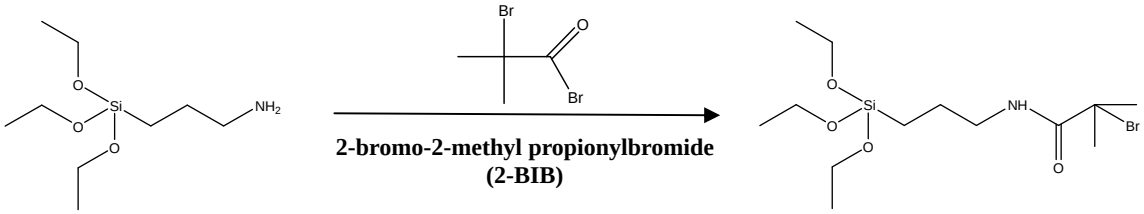


Figure S3. ^{31}P NMR of reference (left) and HEMA-COP and MPC (right).

2. Synthesis and characterization of APTES-Br



Aminopropyl triethoxysilane (APTES)

APTES-Br

Scheme S2 Synthesis of APTES-Br from APTES and 2-BIB.

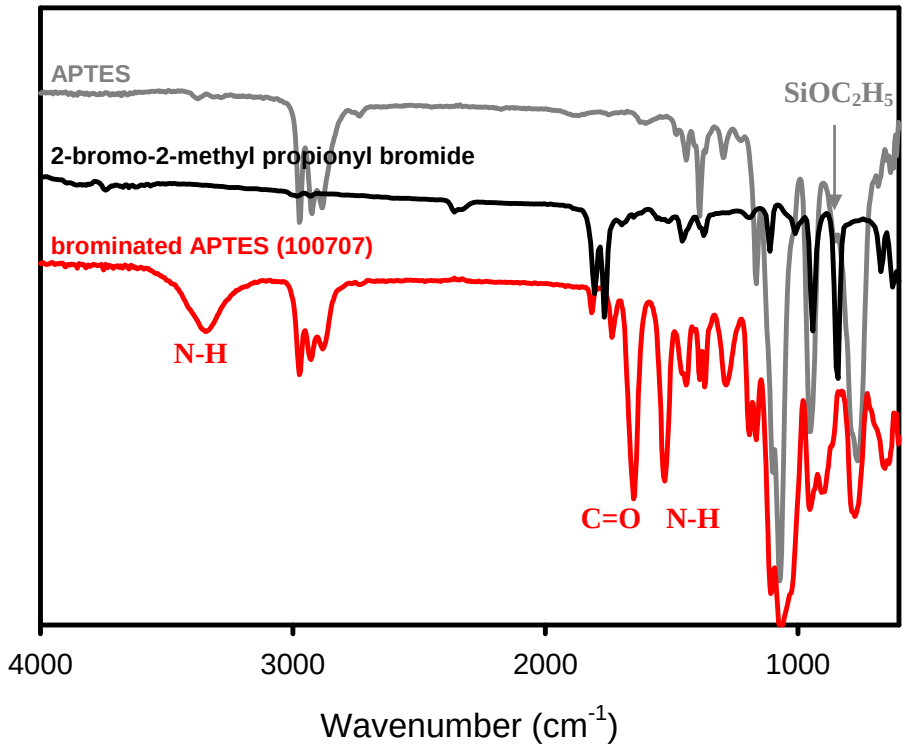


Figure S4. FT-IR spectra of APTES, 2-BIB and APTES-Br.

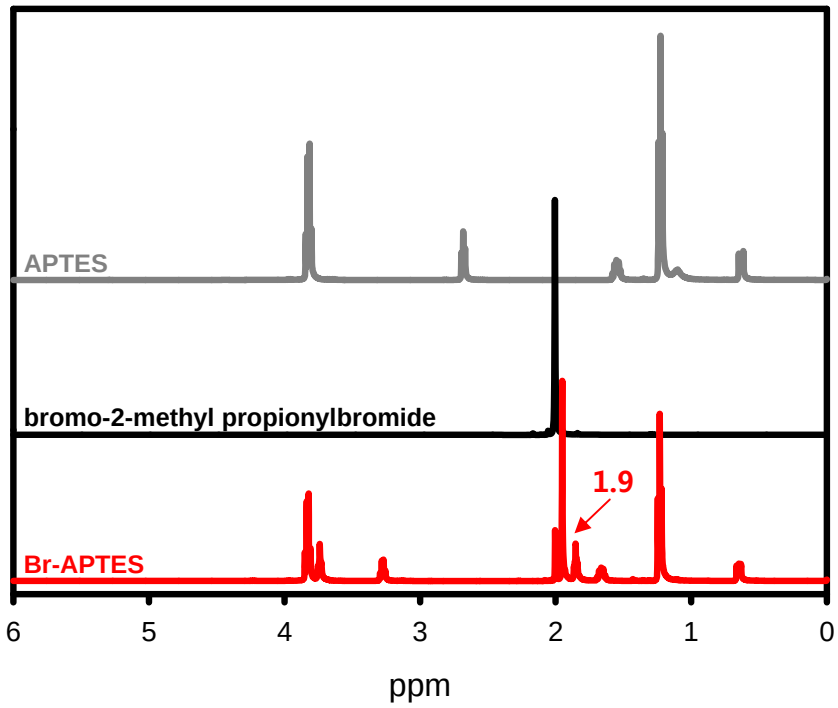


Figure S5. ^{1}H NMR of APTES, 2-BIB and APTES-Br.

3. Preparation of FITC-labeled gadolinium nanoparticles and investigation of the biodistribution behavior

Synthesis of fluorescein labeled Gd_2O_3 core/SiO_2 shell/poly(MPC) nanoparticles

To introduce FITC on the nanoparticles, we added 0.25 g of fluorescein o–methacrylate monomer in the MPC addition step. The procedure was the same as NP1 preparation. After the preparation, the product was washed 5 times with methanol to remove unreacted fluorescein o–methacrylate. We then measured UV-vis absorption by using a UV-visible spectrophotometer (UV-1650PC, Shimadzu Co.) for confocal laser scanning microscopy (CLSM, LSM 710, Carl-Zeiss, Thornwood, NY, USA). The UV-vis spectrum of FITC-labeled Gd_2O_3@SiO_2@PMPC NP solution (the concentration was 2.5×10^{-3} g/mL) is shown in Figure S6. The maximum absorption peak at 488 nm indicates that FITC is introduced on the surface of Gd_2O_3@SiO_2@PMPC NPs.

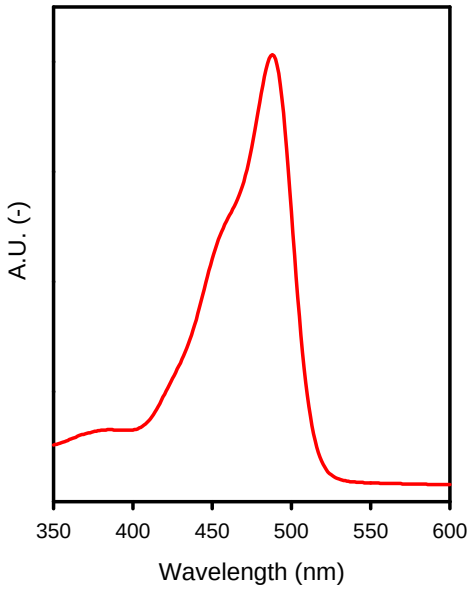


Figure S6. UV-vis spectrum of FITC-labeled Gd_2O_3@SiO_2@PMPC NP solution.

CLSM study with B16F10 cells

CLSM was used to investigate the intracellular distribution of the FITC-labeled Gd_2O_3@SiO_2@PMPC NPs in B16F10 cells. B16F10 cells were prepared as described in the manuscript. The FITC-labeled NPs in cell culture media (100 □μg/mL) were added into B16F10 cells, and which were incubated for 3 h at 37 ^{o}C. The cells were then washed with PBS (pH 7.4) and fixed with 4% (v/v) formaldehyde solution for 10 min. The liquid content was then completely dried and VECTASHIELD mounting medium with 4',6-diamidino-2-phenylindole (DAPI; H-1200, Vector

laboratories, Inc. CA, USA) was added to prevent fading of fluorescence. The CLSM image (a) and (b) in Figure S7 show the B16F10 cells before and after the injection of FITC-labeled NPs, respectively. As shown in Figure S7(a), the black surrounding indicates cytoplasm and the blue globules indicate the DAPI-stained cell nuclei. After the injection of FITC-labeled NPs, one can judge from the green color of FITC dye that FITC-labeled Gd_2O_3@SiO_2@PMPC NPs are localized at the cell nuclei.

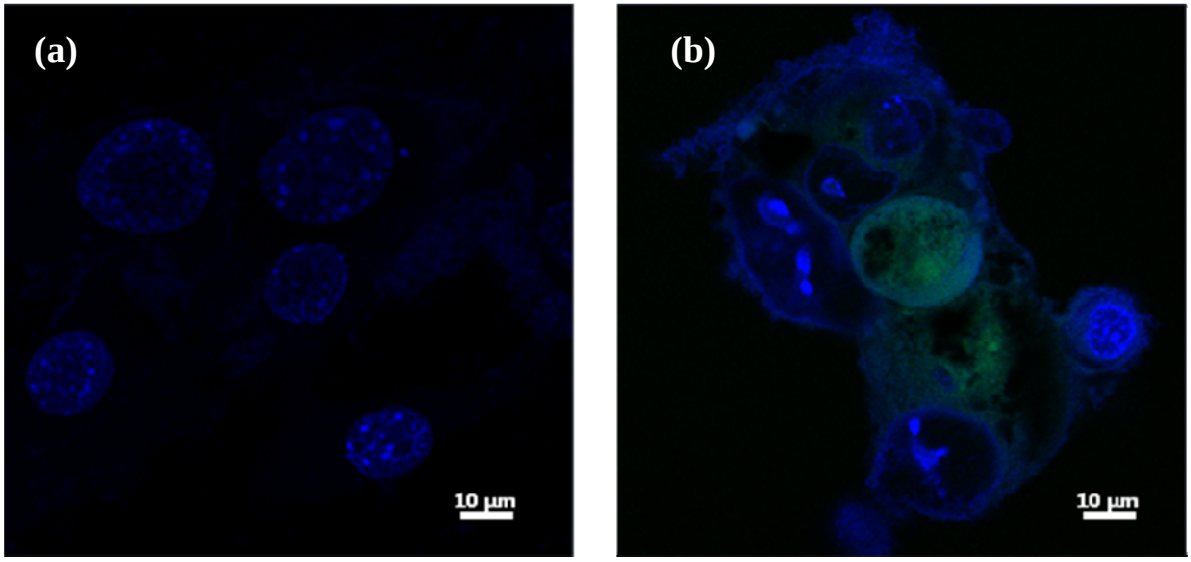


Figure S7. CLSM images of (a) DAPI-stained B16F10 cells and (b) after the injection of FITC-labeled Gd_2O_3@SiO_2@PMPC NPs for *in vitro* cellular uptake study with B16F10 cells.