Supplementary Information

Multifunctional mesoporous silica nanocomposite nanoparticles
for pH controlled drug release and dual modal imaging

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Experimental section

Synthesis of mesoporous silica nanoparticles (MSN). Monodisperse dye-doped MSN was synthesized using the previously reported method. NaOH (0.35 mL, 2 M) was added to 50 mL of aqueous cetyltrimethylammonium bromide (CTAB, Acros, 99+% solution (0.1 g in 50 mL of water). The mixture was heated to 70 °C, followed by the addition of 0.5 mL tetraethylorthosilicate (TEOS, Acros, 98%) and 50 μL of 3-aminopropyltriethoxysilane (APS)-modified dye solution. After 1 min, 0.5 mL of ethyl acetate (EtOAc, Samchun, 99.5%) was added and the resulting mixture was stirred at 70 °C for 30 sec and then aged for 2 h. The resulting precipitate was collected by centrifugation and washed with copious of water and ethanol. Finally, the pore-generating template, cetyltrimethylammonium bromide (CTAB), was removed by refluxing in acidic ethanol solution. For dye incorporated MSN, modified dye was prepared by stirring fluorescein isothiocyanate (FITC, Aldrich) (4 mg) in 1 mL of ethanolic 3-aminopropyltriethoxysilane (APS, Sigma, 98%) solution overnight in the dark (molar ratio of dye:APS = 1:10), followed by co-condensation of the resulting APS modified dye with TEOS during the MSN synthesis step.

Surface modification of MSN. The surface of MSN was functionalized with Br groups by treatment with 3-bromopropyltriethoxysilane (BPS, Gelest, 98%). After the addition of BPS (40 μL) to the ethanolic MSN colloidal suspension (0.1 mg in 10 mL of ethanol), the mixture was refluxed for 3 h. After centrifugation and washing with ethanol, bromine-functionalized MSN was redispersed in 5 mL of water. Hydrazine (35 wt% in H2O, Aldrich) was added into the dispersion, and then was stirred for 1h, and finally the resulting diamine functionalized MSN was retrieved by centrifugation.
**Ligand exchange of Fe₃O₄ nanocrystals and assembly with MSN.** Monodisperse Fe₃O₄ nanocrystals capped with oleic acid were synthesized in organic solution using the previously reported procedures.¹ 2-Bromo-2-methylpropionic acid (BMPA, Aldrich, 98%) (0.5 g) and citric acid (Samchun) (0.05 g) were dissolved in a mixture of chloroform and DMF (50/50 v/v, 15 mL). The synthesized nanocrystals (15 mg) were dispersed in the BMPA solution and stirred overnight at 30 °C. Finally, the ligand-exchanged nanocrystals were retrieved by centrifugation and redispersed in 5 mL of ethanol. The diamine-functionalized MSN dispersion (1 mL) was reacted with 5 mL of the ligand-exchanged Fe₃O₄ nanocrystals dispersion. The diamine-MSN-FITC-Fe₃O₄ was retrieved by centrifugation and washed with ethanol to remove excess Fe₃O₄ nanocrystals.

**Surface modification with PEG.** The resulting diamine-MSN-FITC-Fe₃O₄ was mixed with 25 mg of methoxy poly(ethylene glycol) succinimidy glutarate (mPEG-SG, MW 5000, Sunbio) dissolved in 5 mL of ethanol. The mixture was stirred overnight at 30 °C to induce covalent bonding between diamine groups on the surface of MSN and succinimidy groups of the PEG. After removal of unreacted mPEG-SG by centrifugation and washing, the resulting product was dispersed in MeOH.

**Drug Loading.** For loading of anticancer drug molecules, surface modified MSN was dispersed in 0.5 mL of methanolic doxorubicin solution (4 mg/mL). The mixture was shaken overnight in the dark to induce pH sensitive imine bonding. After removal of unreacted DOX by centrifugation and extensive washing with methanol and pH 7.4 buffer, the supernatant was collected for UV absorption measurement (JASCO V-550) in order to determine the adsorbed amount of DOX. Amount of DOX was calculated from the peak intensity at 480 nm.

**Investigation of pH sensitive Drug Release.** To evaluate the pH-responsive properties, drug loaded MSN particle (3 mg) was dispersed in 2 mL buffer at various pH conditions from 7.4 to 4.0 (10 mM phosphate buffer (pH 7.4 - 6.0) and 10 mM acetate buffer (pH 5.5 - 4.0)). pH-dependent drug release was monitored by measurement of the UV absorbance intensity of DOX in supernatant solution after centrifugation.

**Fig S1.** TEM images of as-synthesized MSN.

**Fig S2.** $^{13}$C CP-MAS solid state NMR of hydrazine-MSN.
**Fig S3.** FT-IR spectra of (a) MSN, and (b) hydrazine-MSN.

**Fig S4.** In vitro cytotoxicity of hydrazine-MSN-FITC-Fe₃O₄-PEG (blue) and DOX conjugated hydrazine-MSN-FITC-Fe₃O₄-PEG (red) against MDAMB231 cell after 24 h incubation.
**Table S1.** Surface ζ-Potentials of the MSN nanocomposites.

<table>
<thead>
<tr>
<th>Material</th>
<th>ζ-Potential (mV)</th>
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<tbody>
<tr>
<td>MSN-FITC</td>
<td>-29.8</td>
</tr>
<tr>
<td>hydrazine-MSN-FITC</td>
<td>-16.7</td>
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<tr>
<td>hydrazine-MSN-FITC-Fe₃O₄</td>
<td>-16.8</td>
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<tr>
<td>hydrazine-MSN-FITC-Fe₃O₄-PEG</td>
<td>-11.4</td>
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