Table of content entry

A newly developed theranostic agent, nrGO@MSN-ION-PEG-RB was fabricated by nanosize reduced graphene oxide/porous silica nanosheets capped with RB-conjugated iron oxide nanoparticles. The nrGO@MSN-ION-PEG-RB demonstrates combination effect of sonodynamic therapy/sonication-induced hyperthermia and magnetic targeting for treating cancer cells.
Supporting information

A theranostic nrGO@MSN-ION nanocarrier with combination effect of sonodynamic therapy and ultrasound hyperthermia for treating tumor

Note-1. Acronyms list:
The acronyms list was added in the revised manuscript.
low-power FUS (LFUS)
Photodynamic therapy (PDT)
sonodynamic therapy (SDT)
photothermal (PTT)
reactive oxygen species (ROS)
photosensitizer (PS)
sonication-induced hyperthermia (SHT)
magnetic field (MF)
mesoporous silica (MSN)
reduced graphene oxide nanosheet (nrGO)
nanosize reduced graphene oxide/mesoporous silica nanocomposites (nrGO@MSN)
iron-oxide nanoparticles (IONs)
Fe$_3$O$_4$ /nrGO/mesoporous silica nanosheets(nrGO@MSN-ION)
Rose Bengal (RB)
Polyethylene glycol (PEG)
mesoporous silica grown on reduced graphene oxide nanosheet capped with Rose Bengal-PEG-conjugated iron-oxide nanoparticles (nrGO@MSN-ION-PEG-RB)
Note 2. Character of graphene oxide (GO) and reduced graphene oxide (nrGO)

**Atomic force microscope (AFM) image:**

![AFM images](image1)

**Figure S1.** Atomic force microscope (AFM) image of (a) rGO and (b) nrGO (c) size measurement of nrGO.

**Raman spectrum of graphene oxide (GO) and reduced graphene oxide (nrGO):**

Figure S2 showed the Raman spectrum of graphene oxide (GO) and reduced graphene oxide (nrGO) obtained at an excitation wavelength of 532 nm. Generally, the intensity of D peak (1350 cm\(^{-1}\)) in the Raman spectra of GO is comparable to the G peak (1600 cm\(^{-1}\)). In contrast, D/G ratio would increase when GO was transferred to nrGO by thermal reduction. [Ref. 1] Thus, we can confirm that in this experiment, the nrGO used to synthesize nrGO@MSN is reduced graphene oxide but not graphene oxide.

![Raman spectra](image2)

**Figure S2.** Raman spectrum of graphene oxide (GO) and reduced graphene oxide (nrGO)
FTIR spectra of nrGO@MSN, DMSA-Fe$_3$O$_4$ and nrGO@MSN-ION (Figure S3):

For the DMSA-Fe$_3$O$_4$, the typical Fe–O stretch is at 601 cm$^{-1}$, and the peak at 2374 cm$^{-1}$ is assigned to S–H stretching. In addition, The C=O stretches at 1624 cm$^{-1}$ is assigned to the stretching mode of carboxylate due to the interaction of the carboxylate anion with the Fe$_3$O$_4$ surface. For the nrGO@MSN-ION, Si–OH (1085 cm$^{-1}$) in the IR spectrum was identified as MSN due to the same as nrGO@MSN. The C=O stretching mode from the carboxylic acid was also detected, but its intensity was reduced because of amide bond formation. The finding indicates that both the N–H (1538 cm$^{-1}$) and C=O (1636 cm$^{-1}$) bonds were present because of the chemical reaction between the carboxylic acid group of DMSA-Fe$_3$O$_4$ and the amino group of MSN to form the amide linkage.

![FTIR spectra of nrGO@MSN, DMSA-Fe$_3$O$_4$, nrGO@MSN-ION and nrGO@MSN-ION-PEG.](image)

**Figure S3.** FTIR spectra of the nrGO@MSN, DMSA-Fe$_3$O$_4$, nrGO@MSN-ION and nrGO@MSN-ION-PEG.

Small angle X-ray diffraction pattern:

![Small angle X-ray diffraction pattern of nrGO@MSN and nrGO@MSN-ION.](image)

**Figure S4.** Small angle X-ray diffraction pattern of nrGO@MSN and nrGO@MSN-ION.
Nitrogen adsorption–desorption isotherms:

**Figure S5.** Nitrogen adsorption–desorption isotherms of nrGO@MSN and nrGO@MSN-ION

Field-dependent magnetization curves:

**Figure S6.** Field-dependent magnetization curves of as-synthesized Fe₃O₄ nanoparticles and nrGO@MSN-ION nanocomposite at room temperature.
Calibration curve of RB concentration:

**Figure S7.** (a) Calibration curve of RB concentration with the inset showing UV-vis spectra of free RB solution with various concentrations. (b) UV-vis spectrum of nrGO@MSN-ION-PEG and nrGO@MSN-ION-PEG-RB solution.

Ultrasonic images:

**Figure S8.** Typical US images with SonoVue bubble as compared with nrGO@MSN and nrGO@MSN-ION-PEG nanocomposites.

**Table S1. Characteristics of nrGO@MSN and nrGO@MSN-ION nanocomposites**

<table>
<thead>
<tr>
<th>Structure Type</th>
<th>Particle Size (nm)[a]</th>
<th>SBJH(m²/g)[b]</th>
<th>VBJH(cm³/g)[b]</th>
<th>Pore Size (nm)[b]</th>
<th>Fe Conc.[c]</th>
</tr>
</thead>
<tbody>
<tr>
<td>nrGO@MSN</td>
<td>50-100nm</td>
<td>819.14</td>
<td>0.84</td>
<td>1.8</td>
<td>X</td>
</tr>
<tr>
<td>nrGO@MSN-ION-ION</td>
<td>50-100nm</td>
<td>105.47</td>
<td>0.50</td>
<td>2.4</td>
<td>7.4%</td>
</tr>
</tbody>
</table>

[a]From transmission electron microscopy (TEM); [b]Mesopore surface area (S_{BJH}) and mesopore volume (V_{BJH}) calculated by the BJH model from the BET absorption/desorption data. [c]Fe concentration of nanocomposites from ICP-Mass.
Note-3. Histological analysis

Figure S9. Histological analysis of liver, kidney, spleen, and lung collected from the nrGO@MSN-ION-PEG-RB-injected mice with and without application of magnetic field (MF) and control untreated mice.

Table S2. The accumulation ratio of various organs to tumor at 24 h post-treatment with and without magnetic field

<table>
<thead>
<tr>
<th></th>
<th>Lung/Tumor</th>
<th>Liver/Tumor</th>
<th>Spleen/Tumor</th>
<th>Kidney/Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>-MF</td>
<td>1.68</td>
<td>1.56</td>
<td>2.84</td>
<td>1.12</td>
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<tr>
<td>+MF</td>
<td>0.66</td>
<td>0.52</td>
<td>1.11</td>
<td>0.41</td>
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</tbody>
</table>