Supporting Information for

Synergistically Enhanced Upconversion Luminescence in Li⁺-Doped Core–Shell-Structured Ultrasmall Nanoprobes for Dual-Mode Deep Tissue Fluorescence/CT Imaging

Min Hu, Dandan Ma, Yuzhong Cheng, Chengcheng Liu, Zhipeng Zhang, Yanjun Cai, Si Wu and Ruifeng Wang

Department of Chemistry, School of Science, Xi’an Jiaotong University, Xi’an 710049, China

Department of Pathogenic Microbiology & Immunology, School of Basic Medical Sciences, Xi’an Jiaotong University Health Science Center, Xi’an 710061, China

Max Planck Institute for Polymer Research, Ackermannweg 10, 55128 Mainz, Germany

Radiology Dept, Affiliated Hospital of the Shannxi University of Traditional Chinese Medicine, Xianyang 712000, China

Table S1. The concentration of Li⁺ and Na⁺ over different samples determined by ICP-MS.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Li</th>
<th>Na</th>
<th>(n_{Li}/n_{Na})%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li_{0.04}</td>
<td>3.684</td>
<td>5021</td>
<td>0.24</td>
</tr>
<tr>
<td>Li_{0.07}</td>
<td>5.516</td>
<td>3746</td>
<td>0.48</td>
</tr>
<tr>
<td>Li_{0.10}</td>
<td>12.84</td>
<td>3009</td>
<td>1.40</td>
</tr>
<tr>
<td>Li_{0.15}</td>
<td>27.17</td>
<td>2351</td>
<td>3.79</td>
</tr>
<tr>
<td>Li_{0.30}</td>
<td>76.7</td>
<td>4202</td>
<td>5.99</td>
</tr>
</tbody>
</table>

The exact amount of doped Li⁺ are determined by ICP-MS. As shown in Table S1. The concentration of measured Li⁺ exhibits same change trend with the incensed amount of LiOH precursors, the percentage of Li to Na also increased as was designed, indicating the successful doping of Li⁺ in NaLuF₄:Yb,Tm system.

S.1 Cytotoxicity Assay.
The cytotoxicity of COC-Li0.07-Lu:Tm@Lu nanoparticles was studied on SMMC 7721 cells utilizing CCK-8 assay. The SMMC 7721 cells were plated in 96-well flat-bottomed plates with 5×10^4 cells per well and cultured in RPMI 1640 (Roswell Park Memorial Institute’s Medium) supplemented with 10% FBS at 37 °C in a humidified incubator (5% CO2). After culturing overnight, the cells were washed with FBS-free RPMI 1640 solutions and then incubated with a specific concentration of COC-Li0.07-Lu:Tm@Lu (50, 100, 200, 400 mg/mL) in FBS-free RPMI 1640 solution (100 μL/well) for 24 h at 37 °C. Subsequently, 10 μL CCK-8 reagent (5 mg/mL) was added to each well and incubated for another 4 h at 37 °C. The absorbance was measured at 450 nm using a monochromator-based multifunction microplate reader.

![Figure S1. Viability of SMMC-7721 cells incubated with COC-Li0.07-Lu:Tm@Lu (50-400 μg/mL) for 24 h by the standard CCK-8 assay.](image)

In vitro test was carried by using human breast cancer cells over 24 h. As it can be observed in Figure 1, the viability of SMMC-7721 cells haven’t show obviously change when incubated for 24 h with COC-Li0.07-Lu:Tm@Lu nanoparticles over a wide concentration range (0-400 μg/mL), indicating negligible biological toxicity of the as decorated COC-Li0.07-Lu:Tm@Lu nanoparticles. The result ensured the feasibility and safety of further in vivo test.
S2. Histological test

SD rat were divided into two groups. SD rat in the first group were injected with COC-Li$_{0.07}$-Lu:Tm@Lu for 14 days and were denoted as the test group. The untreated group was considered the control group. The heart, liver, spleen, lung, and kidney were collected from both groups. These organs were stained with hematoxylin and eosin (H&E) and investigated by an optical microscope.

![H&E-stained tissue sections](image)

**Fig. 2.** H&E-stained tissue sections including heart, liver, spleen, lung, and kidney achieved from SD rat without injection and 14 days after injection of SD rat

A histological analysis of COC-Li$_{0.07}$-Lu:Tm@Lu NPs was conducted by observing the pathological sections of the heart, liver, spleen, lung, and kidney of mice from the control and treated groups for 14 days. Compared with the control group, no noticeable tissue damages on the organs were observed. Therefore, COC-Li$_{0.07}$-Lu:Tm@Lu NPs present low toxicity and good biocompatibility in vivo.