Supporting Information

Radioactive lutetium metallofullerene $^{177}Lu_xLu_{(3-x)}N@C_{80}$ - PCBPEG derivative: a potential tumor-targeted theranostic agent

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Experimental Section:

1. Synthesis and purification of $Lu_3N@C_{80}$

The endohedral metallofullerne $Lu_3N@C_{80}$ was synthesized in a quartz Kräschmer-Huffman electric generator as reported before. In brief, graphite rods of 8 mm diameter, 150 mm length were core-drilled and subsequently packed with a mixture of Lu/Ni_2 alloy and graphite powder in a weight ratio of 4:1. These rods were then vaporized in a Krätschmer-Huffman generator under mixed atmosphere of 6 Torr N_2 and 194 Torr He. The resulting soot was Soxhlet-extracted with toluene for 24 h. $Lu_3N@C_{80}$ was isolated from various empty fullerenes and other lutetium

metallofullerenes by multi-stage HPLC.

2. HPLC profile of purified $Lu_3N@C_{80}$

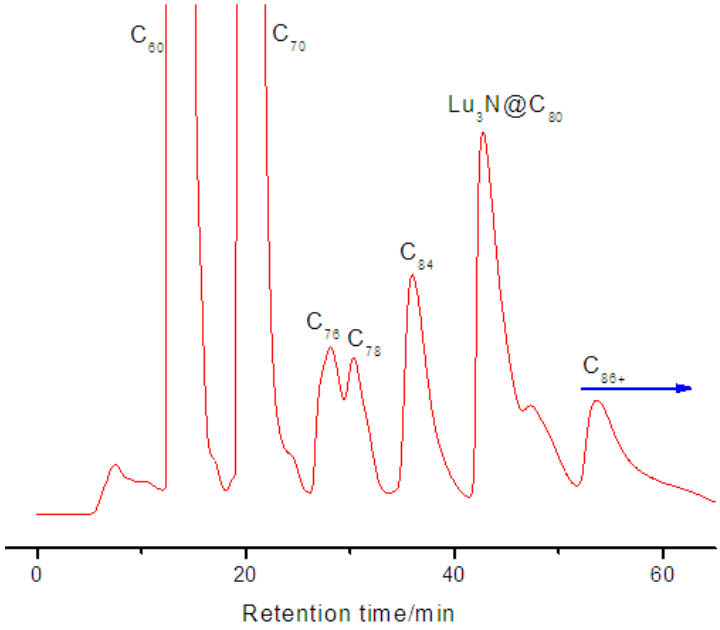

Figure S1. The first stage HPLC profile of toluene extract of the soot containing lutetium endohedral metallofullerenes (Φ20×250 mm Buckyprep column; flow rate 12 mL/min; toluene as eluent).

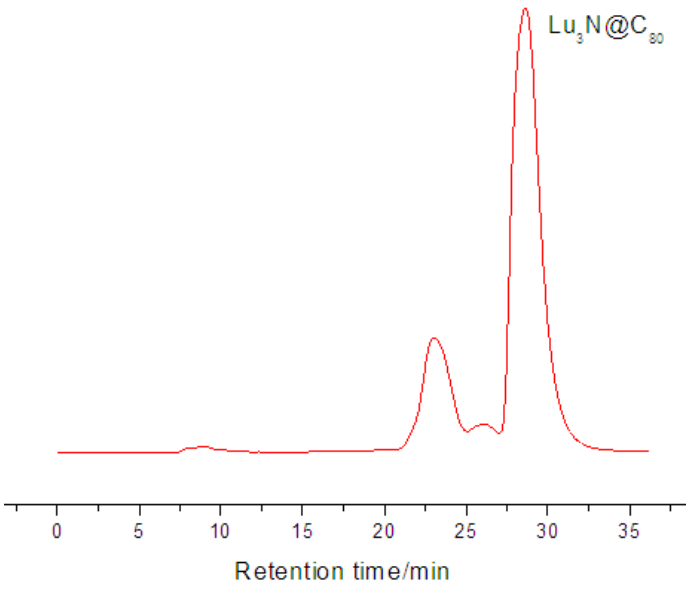

Figure S2. The second stage HPLC profile of isolation of $Lu_3N@C_{80}$ (Φ20×250 mm Buckyprep-M column; flow rate 12 mL/min; toluene as eluent).

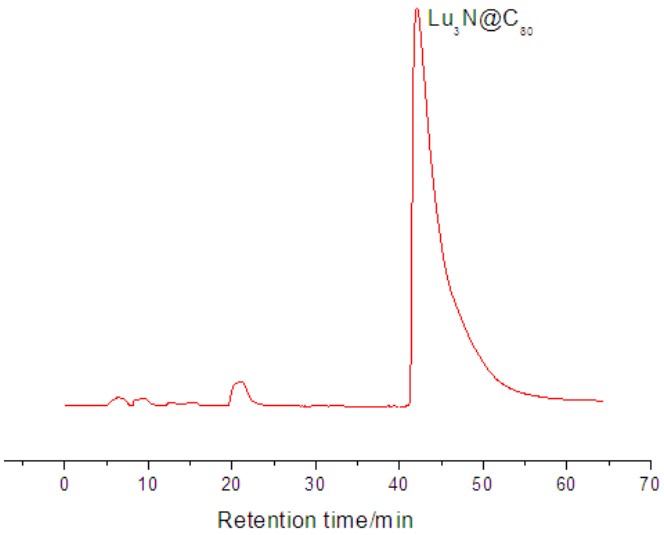

Figure S3. The third stage HPLC profile of isolation of $Lu_3N@C_{80}$ (Φ20×250 mm Buckyprep column; flow rate 12 mL/min; toluene as eluent).

3. MALDI-TOF MS of purified $Lu_3N@C_{80}$

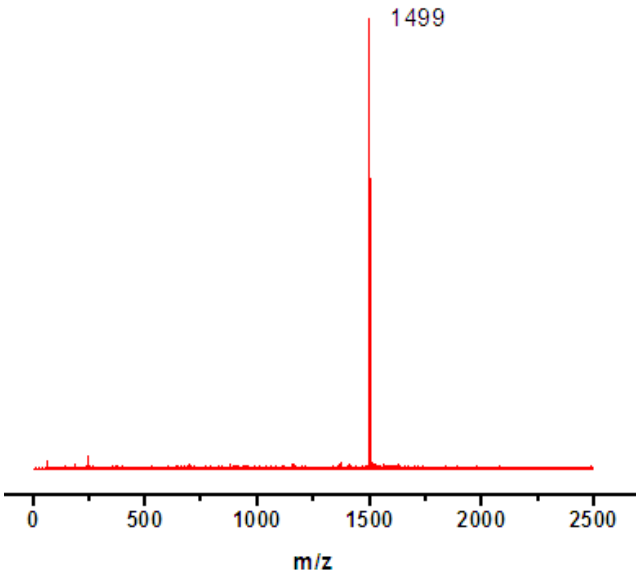

Figure S4. Negative mode MALDI-TOF MS of purified $Lu_3N@C_{80}$

4. Synthesis and of $^{177}Lu_xLu_{(3-x)}N@C_{80}$ by neutron activation

The activation of $Lu_3N@C_{80}$ was taken in a nuclear reactor in the Institute of Nuclear Physics and Chemistry, Chinese Academy of Engineering Physics. 22.0 mg of $Lu_3N@C_{80}$ powders were irradiated by a neutron flux of 6 x 10^{13} n $cm^{-2}s^{-1}$ for the activation of Lu isotopes. After 1 h of irradiation, the sample was first transferred to a bottle for the determination of total ^{177}Lu radioactivity by a γ-ray detector. The activated sample was extracted by toluene under ultrasound and the solution was filtered, the insoluble portion was extracted by toluene several times until no γ-ray signal was detected in the filtered solution. The solution was merged and concentrated, $^{177}Lu_xLu_{(3-x)}N@C_{80}$ was purified and isolated by HPLC. The γ-ray measurement of the dissolved fraction revealed that almost 89% of ^{177}Lu remained in the insoluble fraction, which may ascribe to the effect of the recoil energy associated with the prompt γ-ray emission following the neutron capture.

5. Synthesis and purification of $^{177}Lu_xLu_{(3-x)}N@C_{80}$-PCBM

Methyl 4-benzoylbutyrate p-tosylhydrazone (26.2 mg, 0.07 mmol) was dissolved in 2 mL of pyridine in a dried two-necked flask provided with an Ar inlet and a magnetic stirring bar. Then, NaOMe (3.8 mg, 0.07 mmol) was added, and the mixture was stirred for 15 min. The solution of ~2.1 mg (1.4 μmol) of $Lu_3N@C_{80}$ in 18 mL of toluene was added, and the homogeneous reaction solution was stirred at 100℃ for 25 min, concentrated and purified by HPLC (Φ20×250 mm Buckyprep column; flow rate 12 mL/min; toluene as eluent). The eluent of the $Lu_3N@C_{80}$-PCBM appeared at ca.15 min and the unreacted $Lu_3N@C_{80}$ fraction was at ca. 45 min. The yield was calculated to be about 71%, and the desired product was about 1.6 mg.

6. Synthesis and purification of $^{177}Lu_xLu_{(3-x)}N@C_{80}$-PCBA

To the solution containing $^{177}Lu_3N@C_{80}$-PCBM (1.6 mg, 0.99 mol) in toluene (10 mL)

was added acetic acid (6 mL) and concentrated hydrochloric acid (2 mL). The mixture was heated under reflux overnight. The solvent was removed in vacuo and the precipitate was washed with methanol several times. MALDI-TOF MS and γ-detector showed that the hydrolysis efficiency was nearly 100%.

7. MALDI-TOF MS of purified $^{177}Lu_xLu_{(3-x)}N@C_{80}$-PCBA

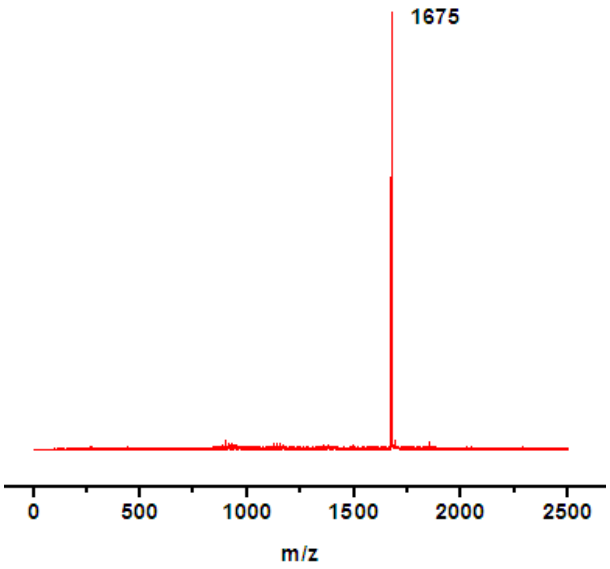

Figure S9. Negative mode MALDI-TOF MS of purified $^{177}Lu_xLu_{(3-x)}N@C_{80}$-PCBA.

8. Synthesis and purification of $^{177}Lu_xLu_{(3-x)}N@C_{80}$-PCBPEG

1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride / N-Hydroxysuccinimide (5 / 5 mg) was added to the chlorobenzene (10 mL) containing $^{177}Lu_3N@C_{80}$-PCBA and ultrasonicated for 20 min. Then mPEG(5000)-NH_2 (100mg, 20 μmol) was added to the above solution. The resulting solution was stirred for 12 h in reflux. The resulting product was purified by a sephadex-25 column to remove the excessive PEG and impurities. The size of the material was tested by dynamic light scattering (DLS) in the physiological saline, and the result showed that the size of most of nanoparticles

centered at ca. 144 nm.

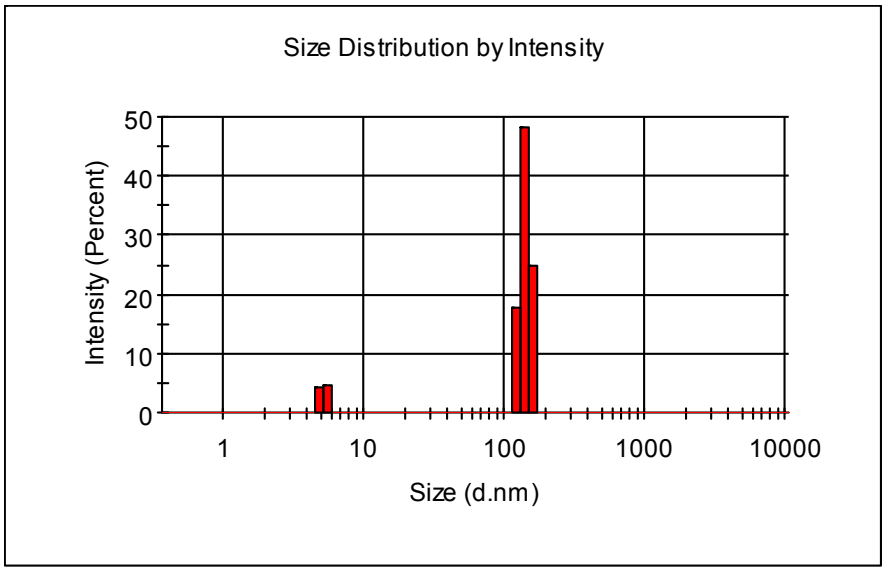

Figure S10. The size distribution of the material in physiological saline(DLS).

9. Blood circulation time of the material.

At different time points (0.5, 1, 5, 12, 24, 48h) of post-injection, the 6 groups of mice were sacrificed successively. From the obtained blood metabolic data below, we can see that at the time point of 0.5 h post-injection, the concentration detected in the blood was at (41.07 ± 1.98) %ID per gram, and from this point, the concentration in the blood reduced gradually. At about 9.5 h post-injection, the data was down to about 20.5 %ID per gram, this meant that the blood half life was about 9 hours. What's more, at the time point of 48 h post-injection, the concentration in the blood was still (3.04 ± 0.34) %ID per gram. Taking into account the metabolic time of nano materials, this is a relatively long blood circulation time.

Figure S11. The concentration of the material in blood post-injection.