Theranostics

Supporting Information

Targeted Mesoporous Iron Oxide Nanoparticles-Encapsulated Perfluorohexane and a Hydrophobic Drug for Deep Tumor Penetration and Therapy

Yu-Lin Su, Jen-Hung Fang, Chia-Ying Liao, Chein-Ting Lin, Yun-Ting Li, Shang-Hsiu Hu*

Department of Biomedical Engineering and Environmental Sciences,
National Tsing Hua University, Hsinchu 300, Taiwan

E-mail: shhu@mx.nthu.edu.tw

Synthesis of Mesoporous Iron Oxide Nanoparticles (MIONs) without oleic acids. In brief, 10 mmol of iron(III) chloride hexahydrate ($FeCl_3 \cdot 6H_2O$, Acros) and 20 mmol of sodium acetate anhydrous (NaAc, Aldrich) were dissolved in 10 ml of ethylene glycol (EG, J. T. Baker) to form a clear solution. Then, the mixture was mixed at 60 ^oC for 24 hours to give a homogeneous solution. The mixture was replaced to a Telfon-lined stainless steel autoclave for the hydrothermal reactions at 220 ^oC for 8 h. After the reaction, the autoclave was cooled down to room temperature for another 3 h. The magnetic particles were collected by centrifugation at 7,000 rpm for 12 min and washed with excess ethanol 3 times afterwards. Before characterization and application, the particles were dried under vacuum overnight at room temperature. The morphologies of MIONs were characterized by a field emission scanning microscope (FE-SEM, JEOL-6700, Japan) as shown in **Figure S1**.

Magnetic Property and Stability of Lf-MIONs. The magnetization of dried particles was exhibited by magnetization (*M*)-field (*H*) curves, where the saturation at a field that is smaller than that observed in MION (**Fig. 2h**). The result shows a stronger inter-particle interaction for the MIONs. The lower magnetization of OA-MIONs and Lf-MIONs is due to the concentration dilution by oleic acid or lactoferrin. Based on the magnetic particle, OA-MIONs and Lf-MIONs have the identical magnetization property as that of MIONs. These properties indicate that the MION respond to the magnetic field in a similar way as OA-MIONs and Lf-MIONs but with a higher magnetic susceptibility. Furthermore, the stability of Lf-MIONs during a 4 °C storage was investigated in solution. As shown in the **Figure S2**, the magnetic property of Lf-MIONs after 3 weeks was compared with that of the original, exhibiting only slight difference of less than 4 %.

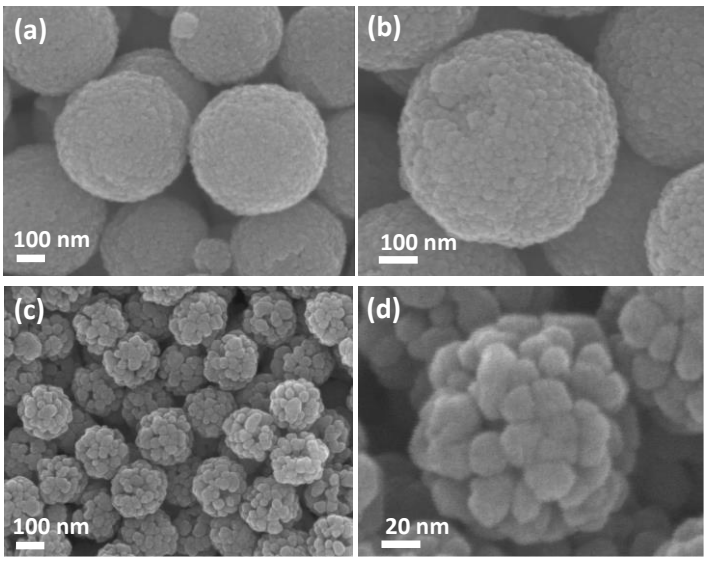

Figure S1 SEM images of resulting MIONs prepared by (a, b) without OA and (c, d) with OA in the synthesized processes.

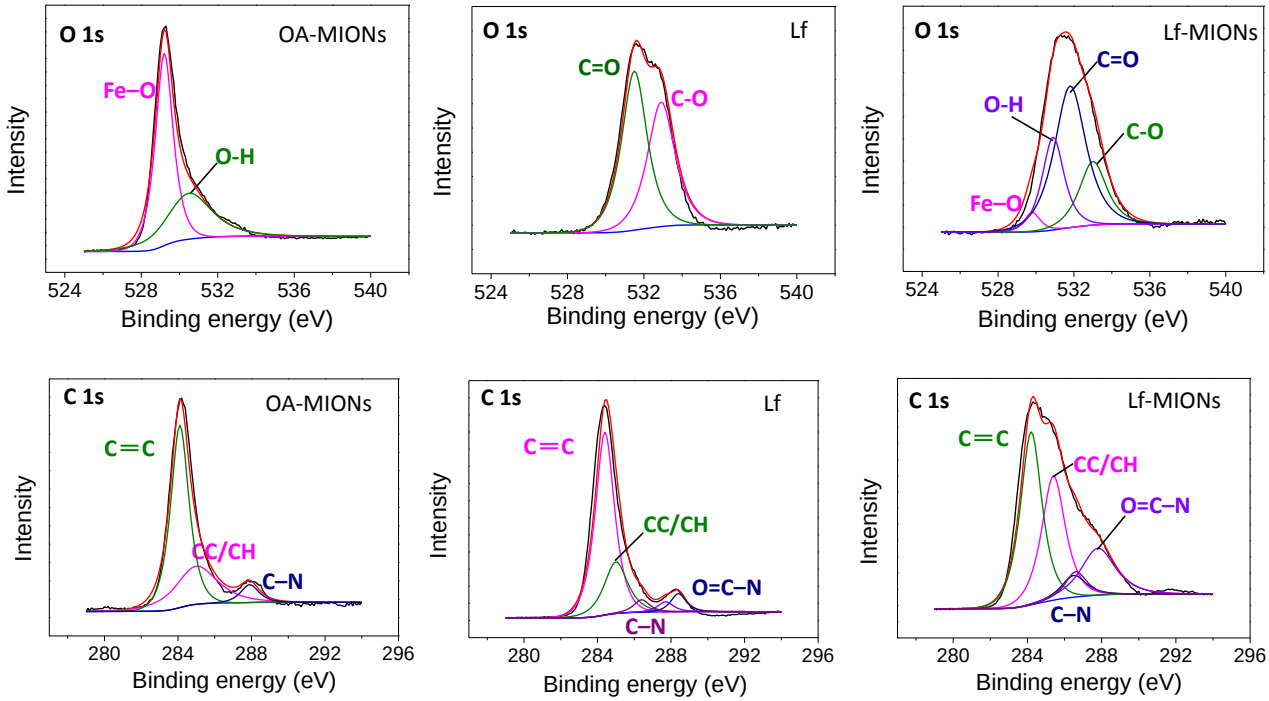

Figure S2 XPS survey scan spectra of OA-MIONs, lactoferrin (Lf), and Lf-MIONs.

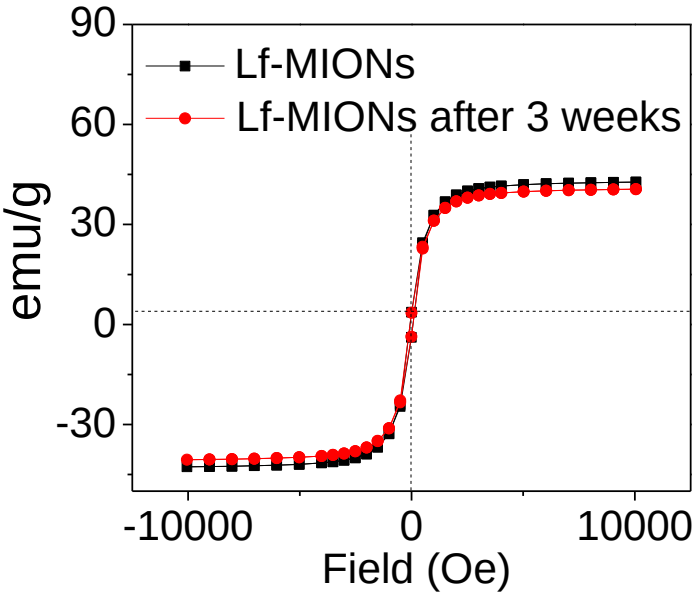

Figure S3 Field-dependent magnetization curve of Lf-MION after storage at 4 °C for 3 weeks. There was no significant change in the physical characteristic.

Table S1 The pore structure parameters before and after PTX loading to OA-MIONs.

Sample	Surface Area (m^2/g)	Pore Volume (cm^3/g)	Pore Size (nm)
OA-MIONs	110.6	0.76	18.4
OA-MIONs/PTX	24.2	0.15	15.5

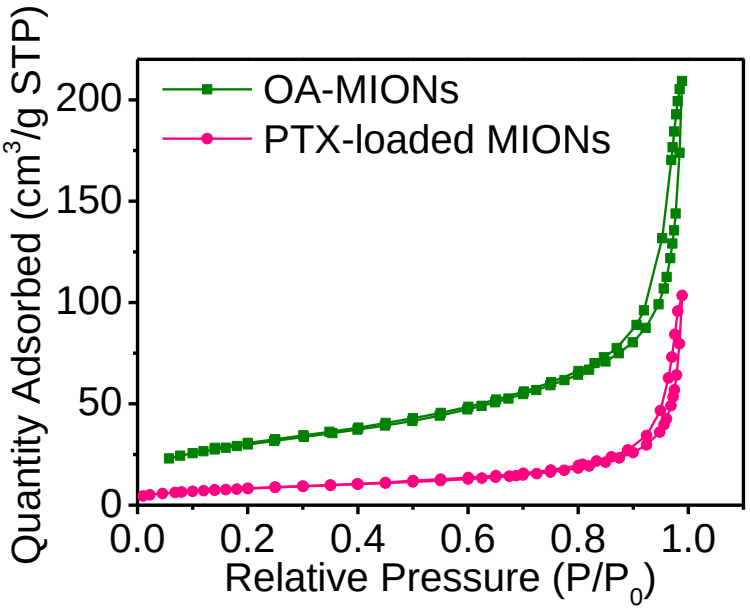

Figure S4 N_2 adsorption–desorption isotherms of OA-MIONs before and after PTX loading.

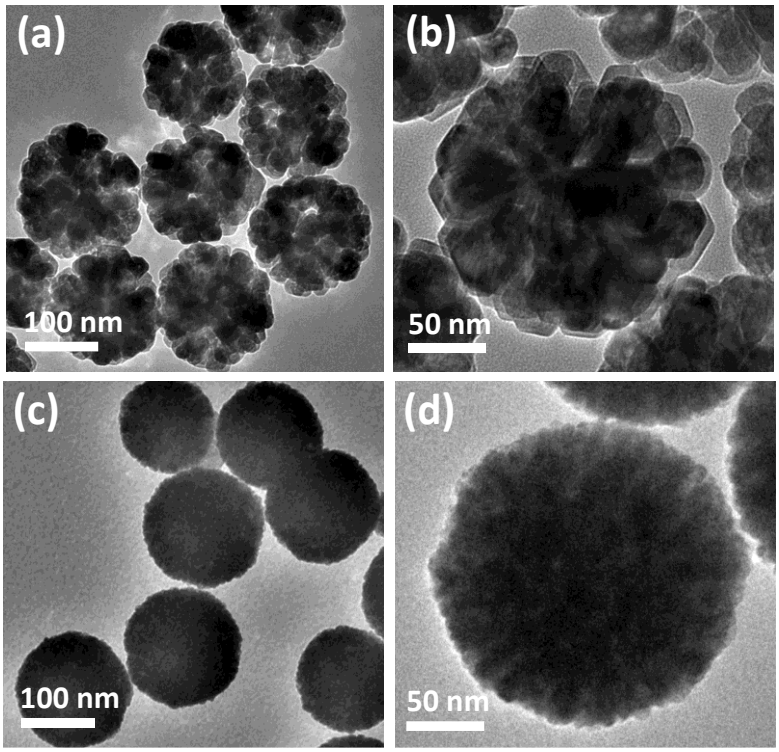

Figure S5 TEM images of OA-MIONs (a, b) before and (c, d) after PTX loading.

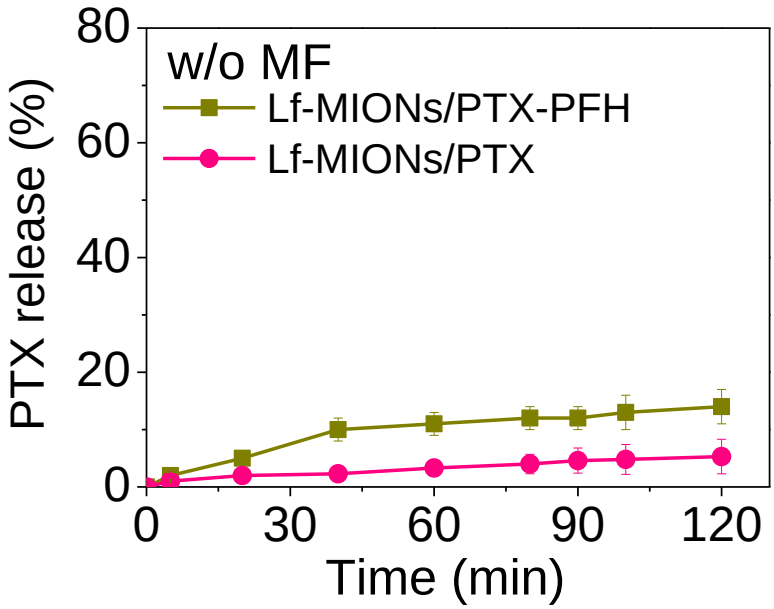

Figure S6 Cumulative PTX release from Lf-MIONs/PTX-PFH and Lf-MIONs/PTX without MF treatment.

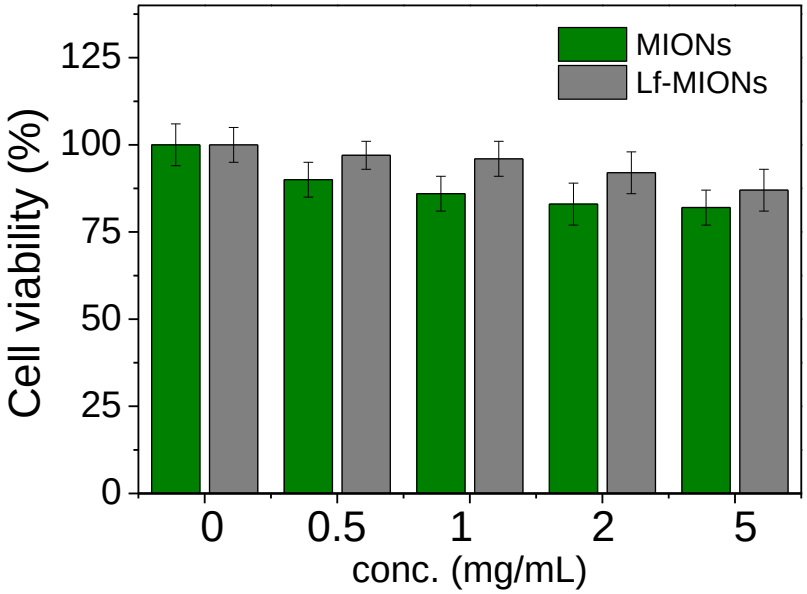

Figure S7 Cell viability of RG2 cells after 24 h incubation with various concentrations of MIONs and Lf-MIONs.

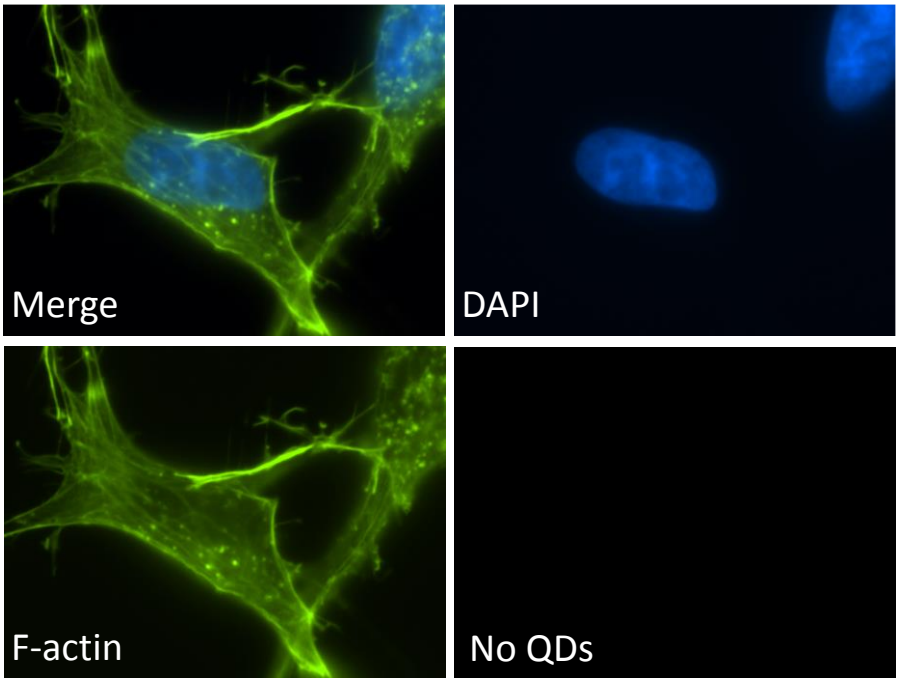

Figure S8 Control experiment on RG2 cells without any particles.

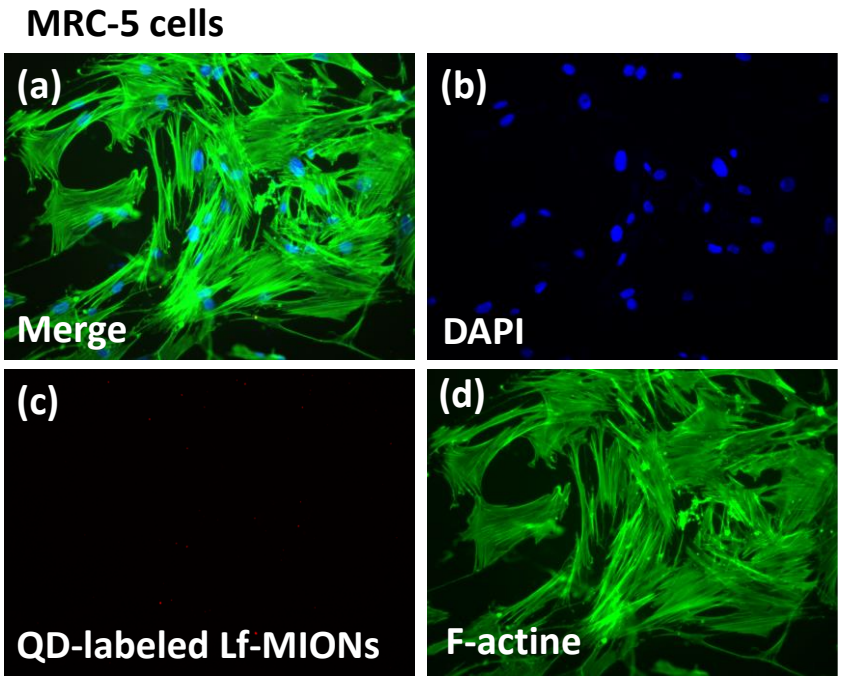

Figure S9 Cellular uptake of quantum dot (QD)-loaded Lf-MIONs in MRC-5 (a human lung fibroblast, normal cell) cells after 2 h of incubation.

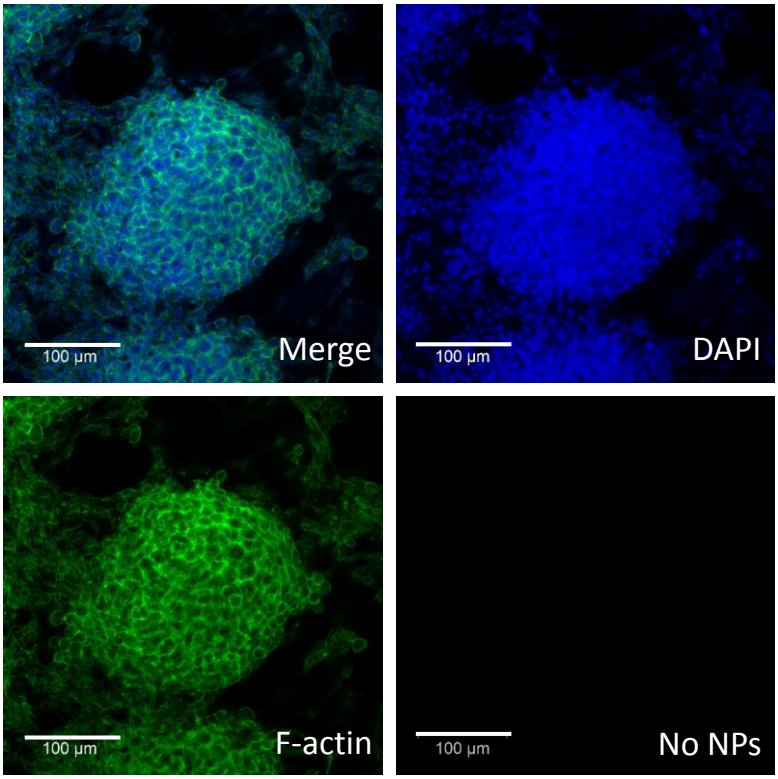

Figure S10 Control experiment on RG2 cells without any particles.

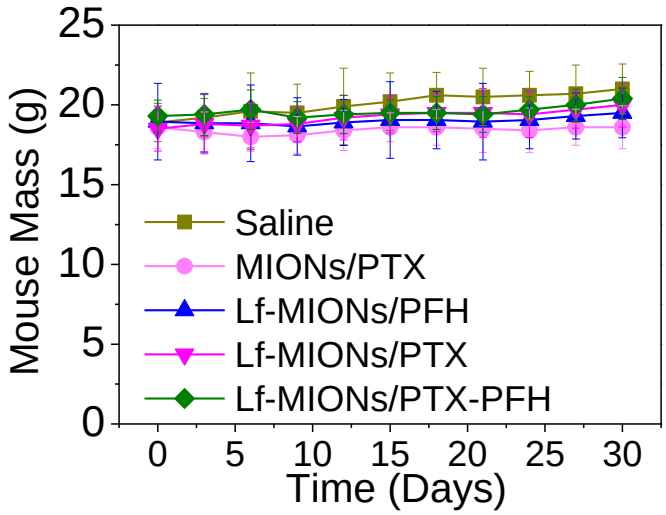

Figure S11 Mouse mass after treating by saline, MIONs/PTX, Lf-MIONs/PTX, and Lf-MIONs/PTX-PFH for 30 days.