Journal Name

ARTICLE

Supporting Information

Oral Administration of Highly Bright Cr^{3+} Doped $ZnGa_2O_4$ Nanocrystals for *in vivo* Targeted Imaging of Orthotopic Breast Cancer

Hanghang Liu[a], Feng Ren[a], Hao Zhang[a], Yaobao Han[a], Huizhu Qin[b], Jianfeng Zeng[a], Yong Wang[a], Qiao Sun[a], Zhen Li[a], Mingyuan Gao[a]*

[a] Center for Molecular Imaging and Nuclear Medicine, State Key Laboratory of Radiation Medicine and Protection, School for Radiological and Interdisciplinary Sciences (RAD-X), Soochow University, Collaborative Innovation Center of Radiation Medicine of Jiangsu Higher Education Institutions

Suzhou 215123, China

Email: zhenli@suda.edu.cn

[b] Medical School of Nantong University, Clinical Medicine

Nantong 226019, China

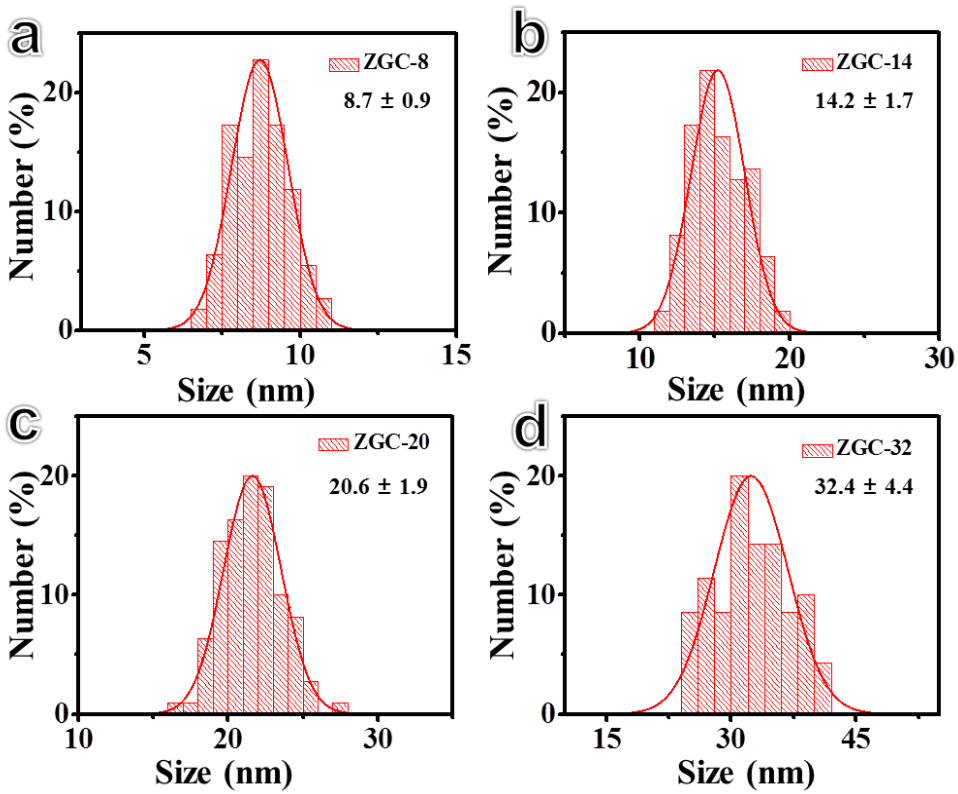

Fig. S1. Particle size distributions of (a) ZGC-8, (b) ZGC-14, (c) ZGC-20, and (d) ZGC-32, respectively.

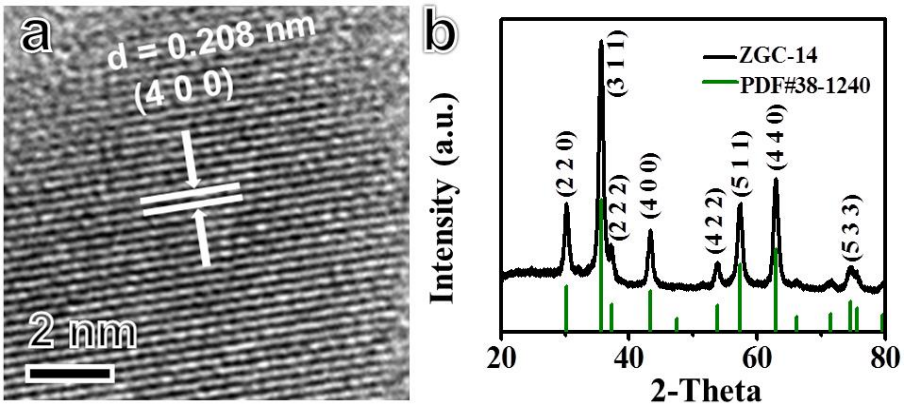

Fig. S2. (a) HRTEM image of typical ZGC nanocrystal; (b) XRD pattern of ZGC-14 in comparison with the standard peaks of $ZnGa_2O_4$ (JCPDS Card No. 38-1240).

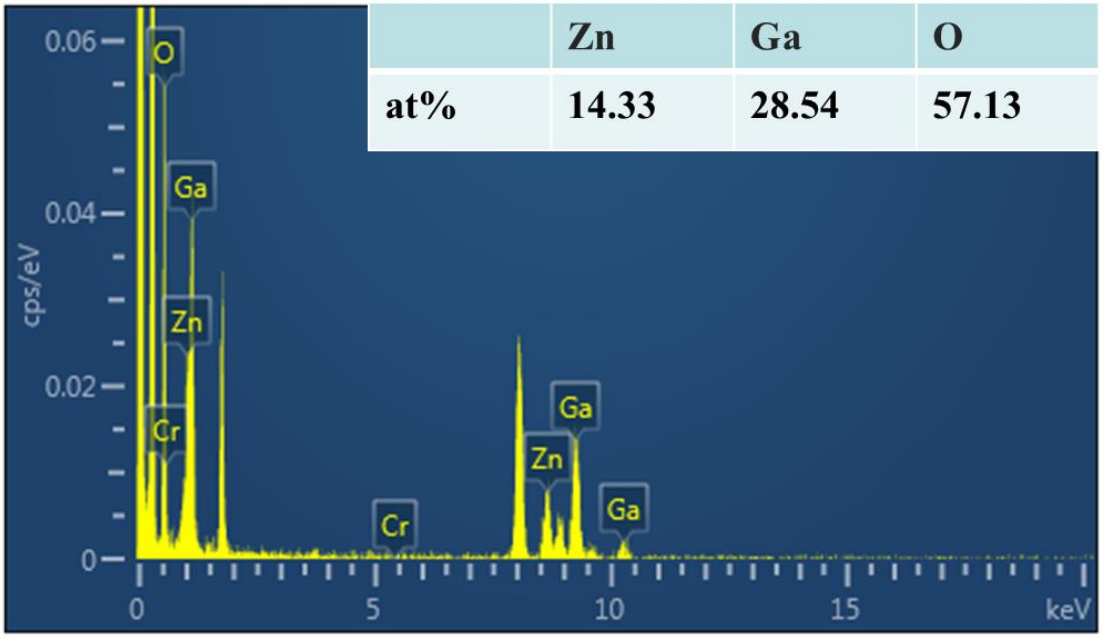

Fig. S3. EDX spectrum of ZGC-14 nanocrystals, with the inset showing the atomic percentages of Zn, Ga, and O.

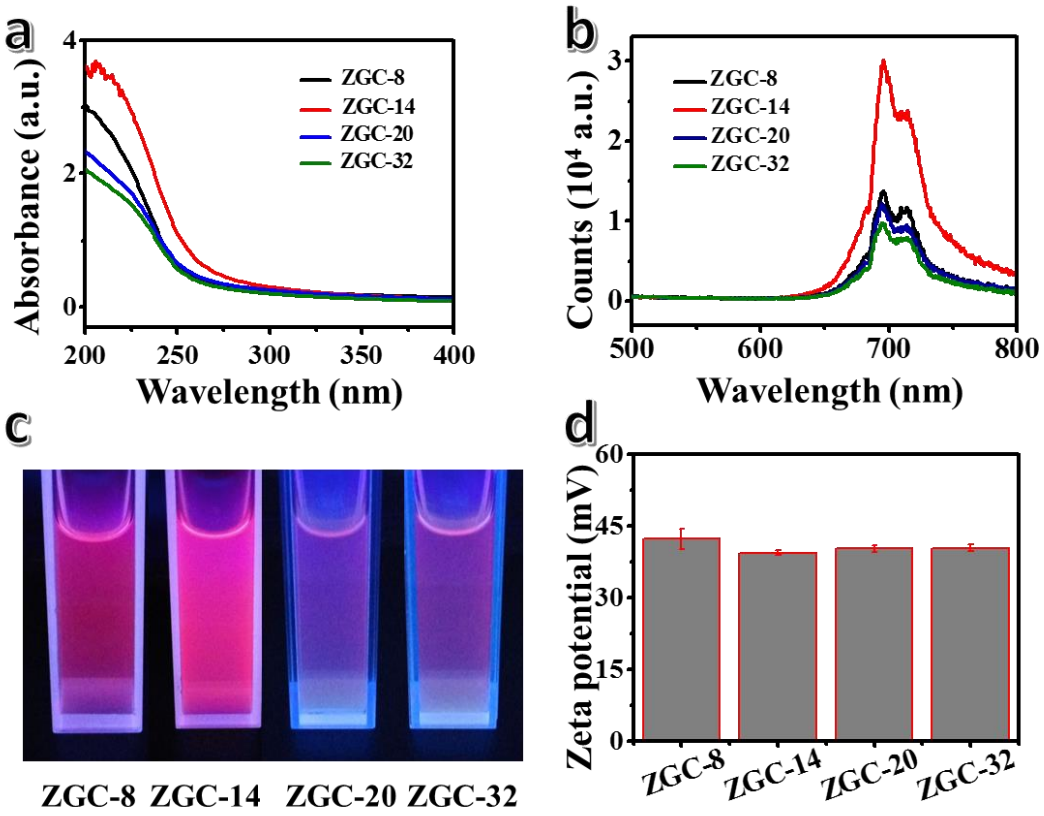

Fig. S4. (a) UV-Vis absorbance and (b) photoluminescence spectra of solutions with different-sized ZGC nanoparticles at a concentration of 0.5 mg/mL; (c) photographs of the fluorescence of the solutions with different-sized ZGC nanocrystals excited with 254 nm UV light at the same time; (d) Zeta potential of different-sized ZGC nanocrystals.

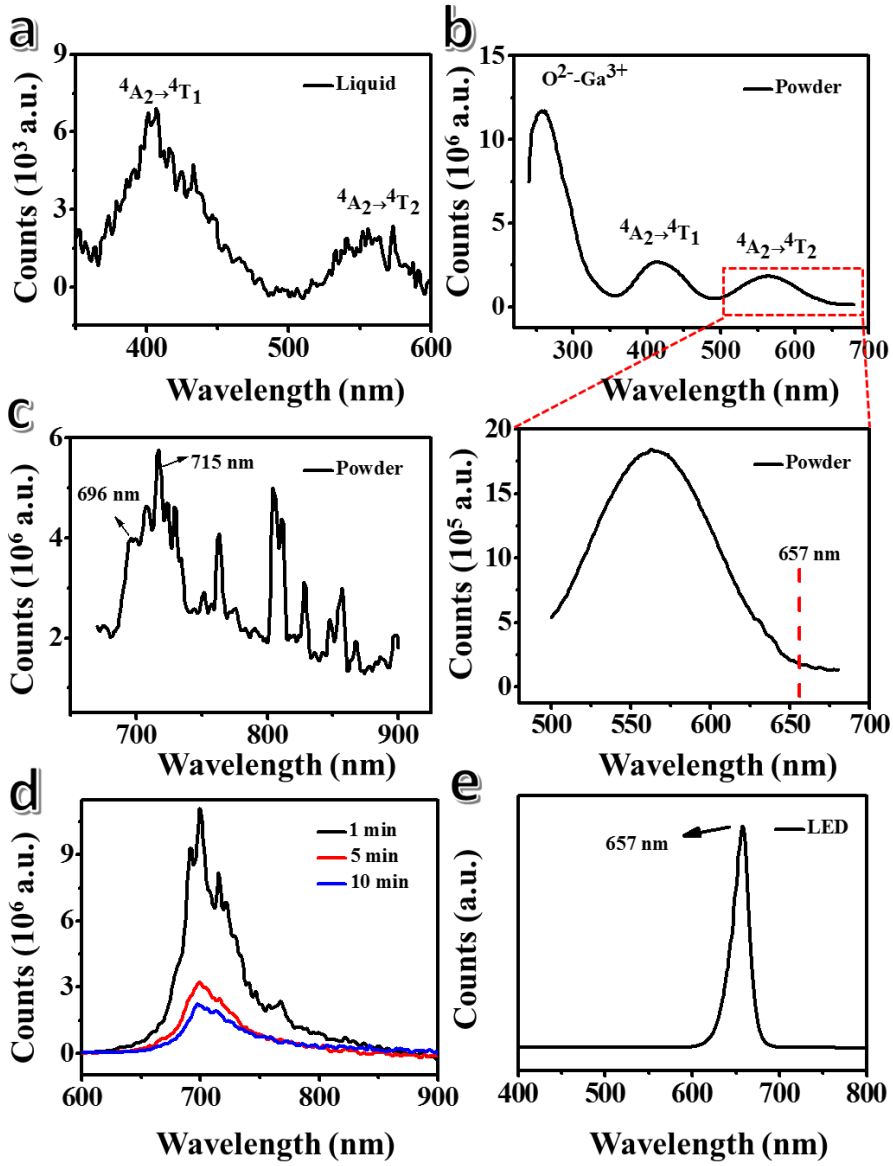

Fig. S5. (a) Excitation spectra of (a) ZGC-14 aqueous solution (0.5 mg/mL) and (b) its solid powder (200 mg); (c) Emission spectrum of ZGC-14 nanocrystals excited at 657 nm and (d) Emission spectra of ZGC-14 nanocrystals measured at different times (*i.e.*, 1 min, 5 min, 10 min) after the excitation light was turned off; (e) spectrum of the LED light used in our experiment.

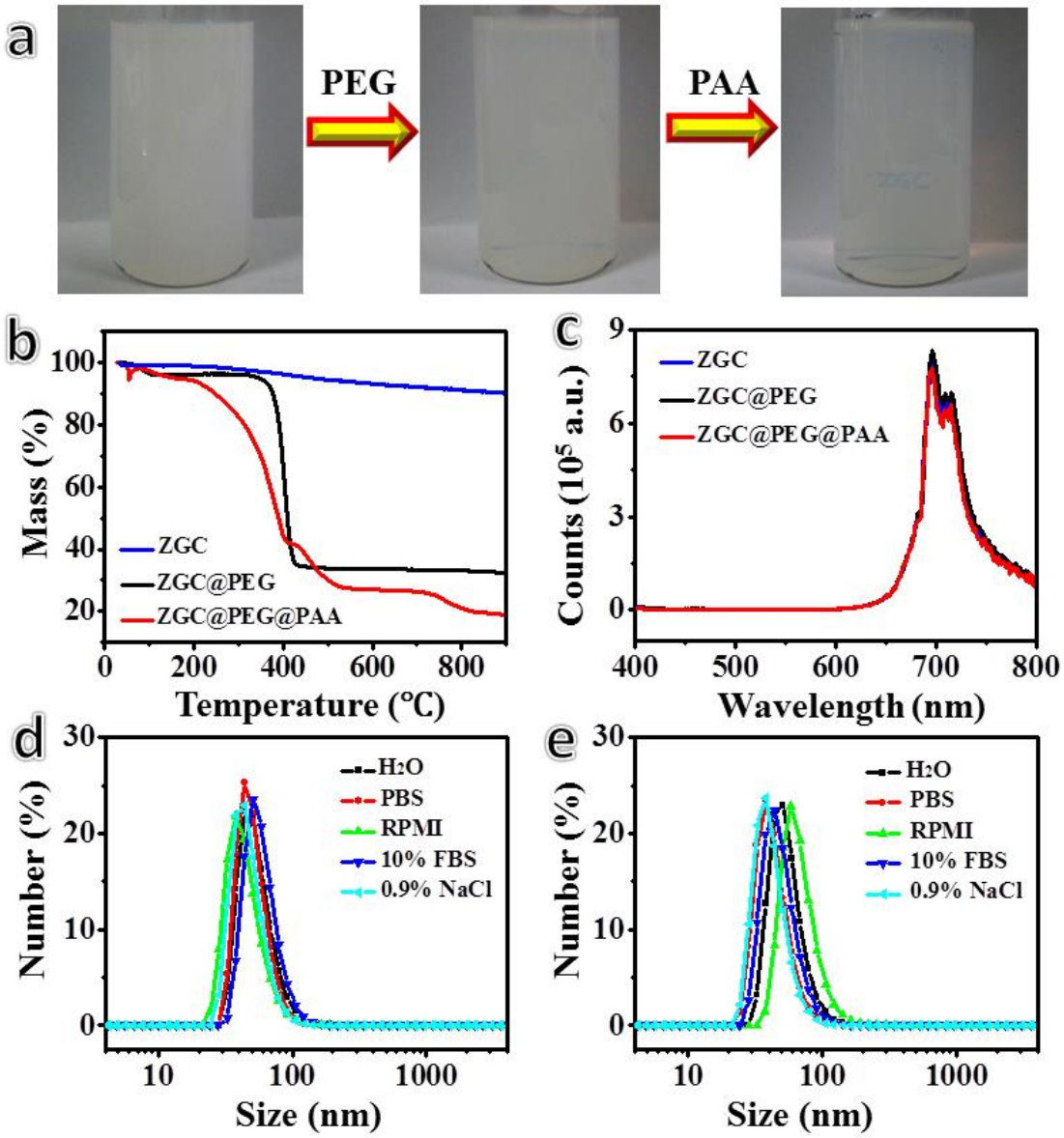

Fig. S6. (a) Photographs of ZGC nanocrystal solution before and after modification with PEG and PAA; (b) TGA curves of ZGC, ZGC@PEG, and ZGC@PEG@PAA nanocrystals; (c) photoluminescence spectra of ZGC, ZGC@PEG, and ZGC@PEG@PAA nanocrystal solutions with the same concentration (0.5 mg/mL); (d-e) hydrodynamic size of ZGC@PEG@PAA nanocrystals dispersed in different media including H_2O, PBS, RPMI medium, and 10% FBS, and 0.9% NaCl for 0 day (d) and 15 days (e).

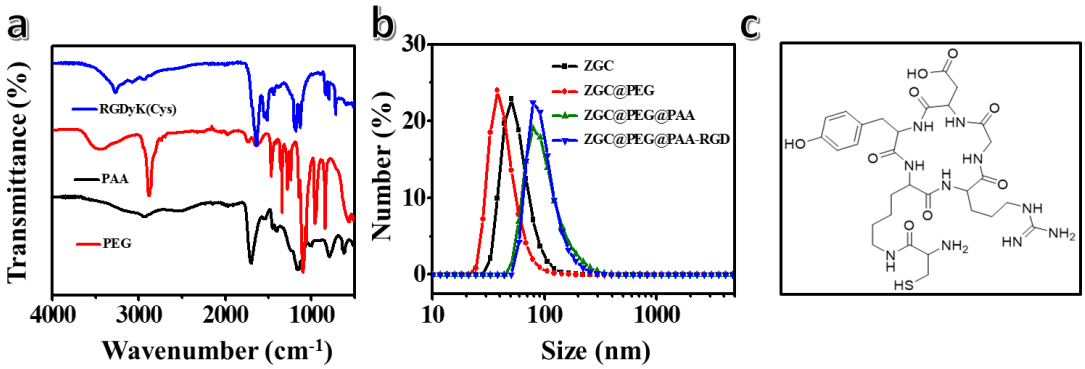

Fig. S7. (a) FTIR spectra of PEG, PAA and c(RGDyK); (b) hydrodynamic size of ZGC-14 nanocrystals conjugated with PEG, PAA and c(RGDyK) peptide. (c) Specific chemical structure of the c(RGDyK).

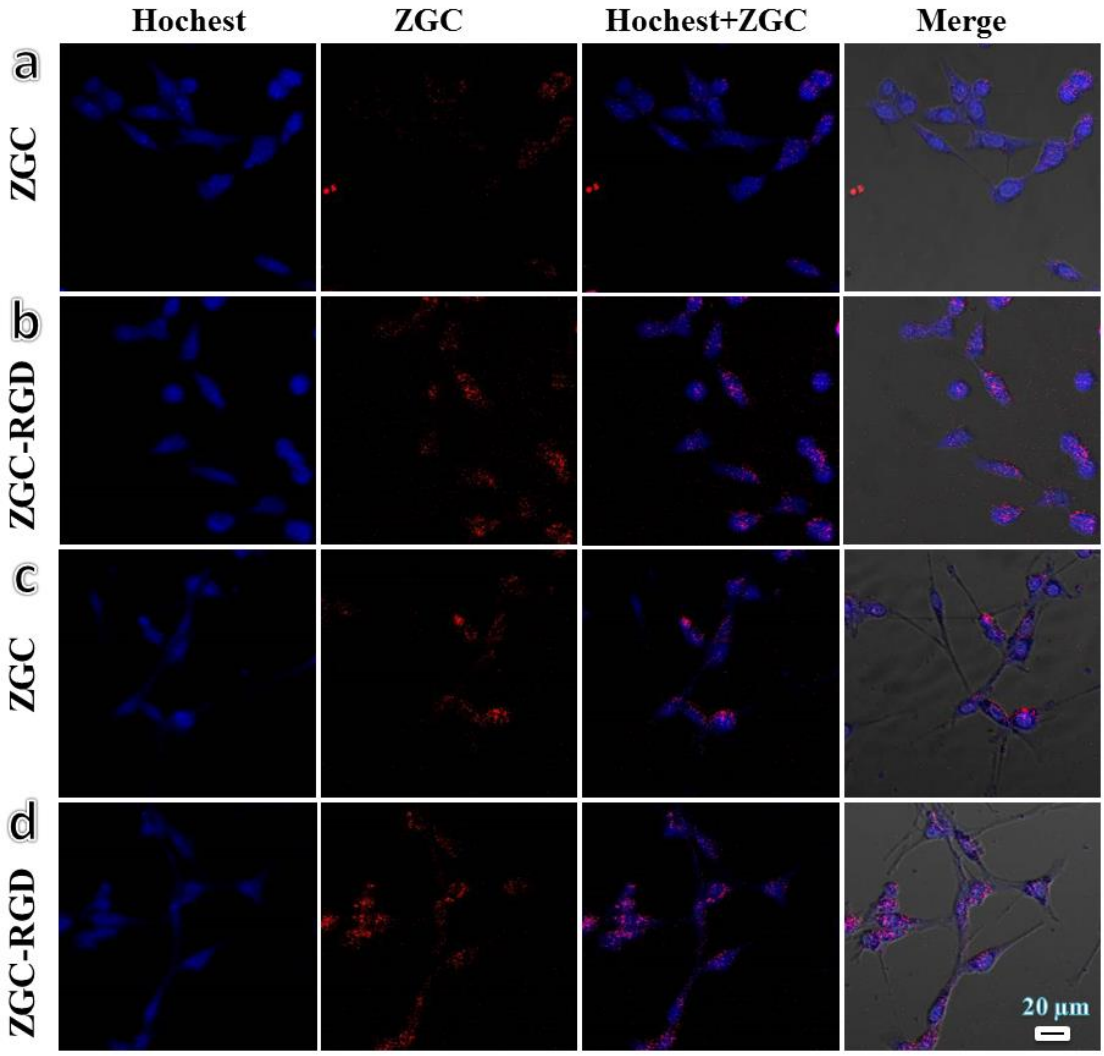

Fig. S8. Confocal fluorescence microscope images of 4T1 (a-b) and U87 cells (c-d) labeled with ZGC@PEG@PAA (labeled as ZGC on the figure) and ZGC@PEG@PAA-RGD (labeled as ZGC-RGD) nanocrystals. Nuclei were stained with Hoechst 33342 in blue, and the ZGC fluorescence in the cells is red.

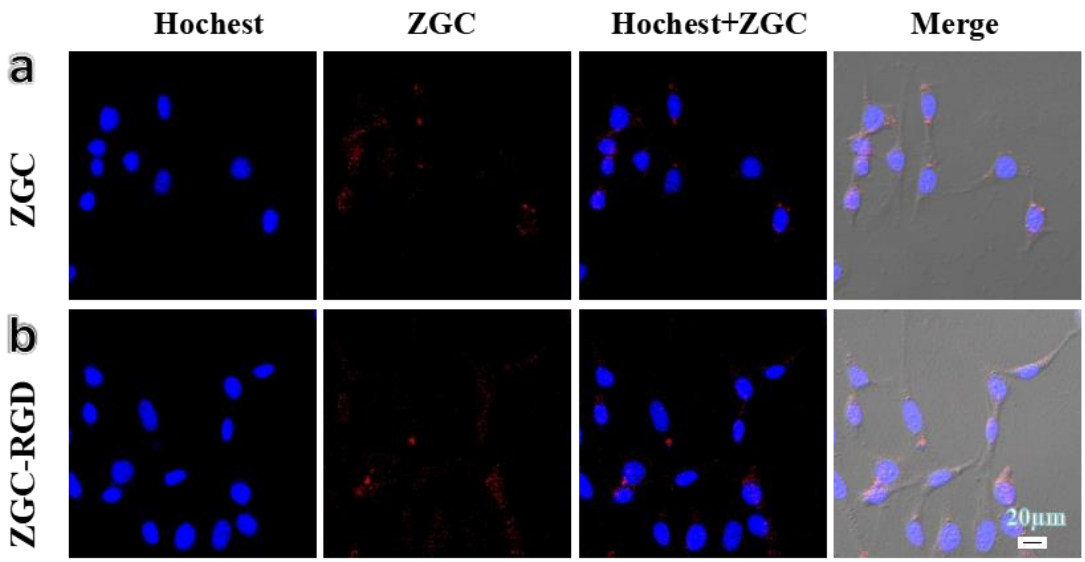

Fig. S9. Confocal fluorescence microscopic images of NIH3T3 cells treated with (a) ZGC@PEG@PAA, (b) ZGC@PEG@PAA-RGD. Nuclei were stained with Hoechst 33342 (blue), ZGC fluorescence in cells (red) was excited by laser of 405 nm.

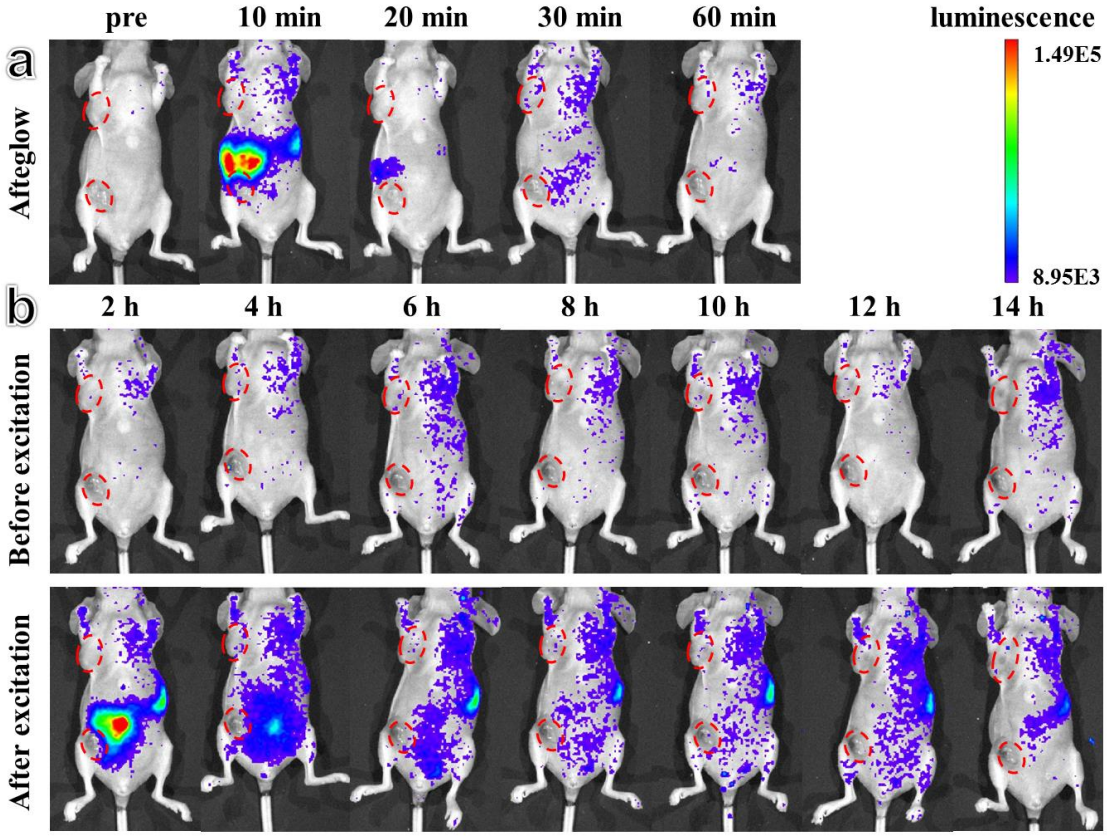

Fig. S10. *In vivo* luminescent images of 4T1 tumor-bearing mice after oral administration of ZGC@PEG@PAA NCs (3.6 mg/mL, 200 µL, excited with 254 nm UV light for 10 min before injection); (a) afterglow luminescence images of mouse in the first 60 min; (b) afterglow luminescence images of mouse irradiated with 657 nm LED light at different times after oral administration. The exposure time during image collection was 60 s.

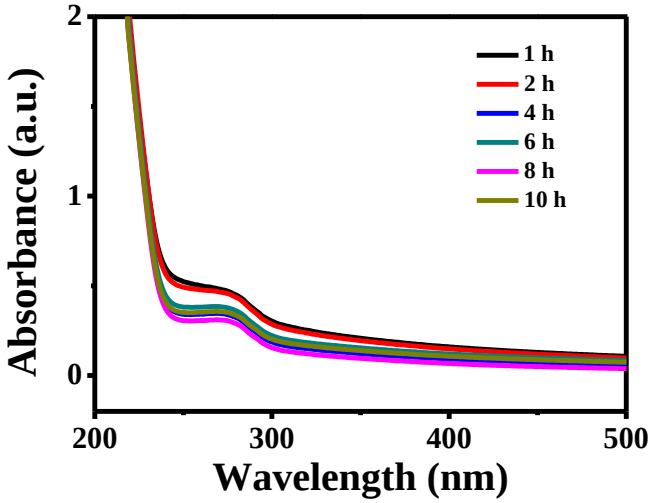

Fig. S11. UV-VIS absorbance of ZGC@PEG@PAA-RGD in an acidic pepsin solution (pH =1-2).

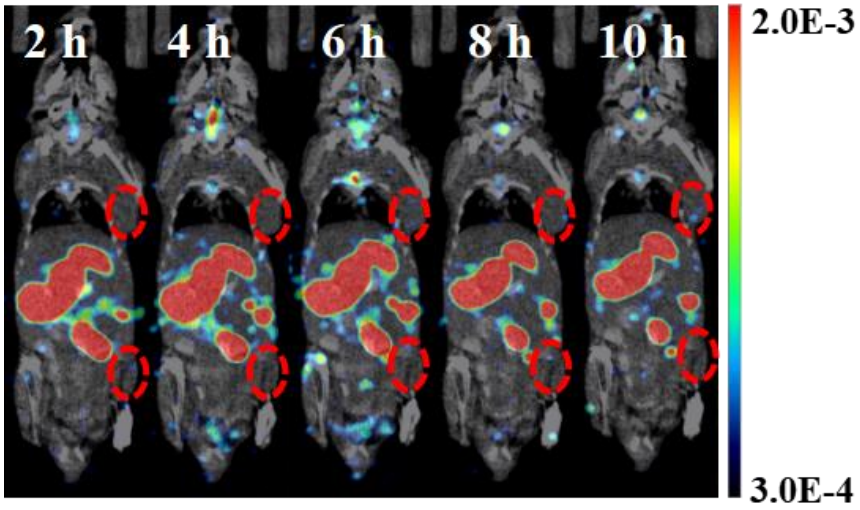

Fig. S12. *In vivo* SPECT/CT images of 4T1 tumor-bearing mice (tumors indicated by the red circles) after oral administration of ^{99m}Tc-labeled ZGC nanocrystal solution.