Supporting Information

Oral Administration of Highly Bright Cr$^{3+}$ Doped ZnGa$_2$O$_4$ Nanocrystals for in vivo Targeted Imaging of Orthotopic Breast Cancer

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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$_2$O$_4$ (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 H₂O, 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.