Design of near-infrared fluorescent bioactive conjugated functional iron oxide nanoparticles for optical detection of colon cancer

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Abstract

Background: Colon cancer is one of the major causes of death in the Western world.[1] Early detection significantly improves long-term survival for patients with the disease.[2] Near-infrared (NIR) fluorescent nanoparticles hold great promise as contrast agents for tumor detection. NIR offers several advantages for bioimaging compared with fluorescence in the visible spectrum, ie, lower autofluorescence of biological tissues, lower absorbance, and consequently deeper penetration into biomatrices.[3]

Methods and results: NIR fluorescent iron oxide nanoparticles with a narrow size distribution were prepared by nucleation, followed by controlled growth of thin iron oxide films onto cyanine NIR dye conjugated gelatin-iron oxide nuclei. For functionalization, and in order to increase the NIR fluorescence intensity, the NIR fluorescent iron oxide nanoparticles obtained were coated with human serum albumin containing cyanine NIR dye. Leakage of the NIR dye from these nanoparticles into phosphate-buffered saline solution containing 4% albumin was not detected. The work presented here is a feasibility study to test the suitability of iron oxide-human serum albumin NIR fluorescent nanoparticles for optical detection of colon cancer. It demonstrates that encapsulation of NIR fluorescent dye within these nanoparticles significantly reduces photobleaching of the dye. Tumor-targeting ligands, peanut agglutinin and anticarcinoembryonic antigen antibodies (αCEA), were covalently conjugated with the NIR fluorescent iron oxide-human serum albumin nanoparticles via a poly(ethylene glycol) spacer. Specific colon tumor detection was demonstrated in chicken embryo and mouse models for both nonconjugated and the peanut agglutinin-conjugated or αCEA-conjugated NIR fluorescent iron oxide-human serum albumin nanoparticles.[4]

Conclusion: Conjugation of peanut agglutinin or αCEA to the nanoparticles significantly increased the fluorescence intensity of the tagged colon tumor tissues relative to the nonconjugated nanoparticles.

References

[1] Franziska A, Ulrike S, The International Journal of Biochemistry & Cell Biology, **12** (2009) 2356-2359.

[2] Majek O, Gondos A, Jansen L, Emrich K, Holleczek B, Katalinic A, Nennecke A, Eberle A, Brenner H, British Journal of Cancer **106** (2012) 1875-1880.

[3] [4] Santra S, Malhotra A., Wiley Interdiscip Rev Nanomed Nanobiotechnol,**3** (2011) 501–510.

[4] Corem-Salkmon E, Perlstein B, Margel S, International Journal of Nanomedicine**, 7** (2012) 5517-5527.

Figures

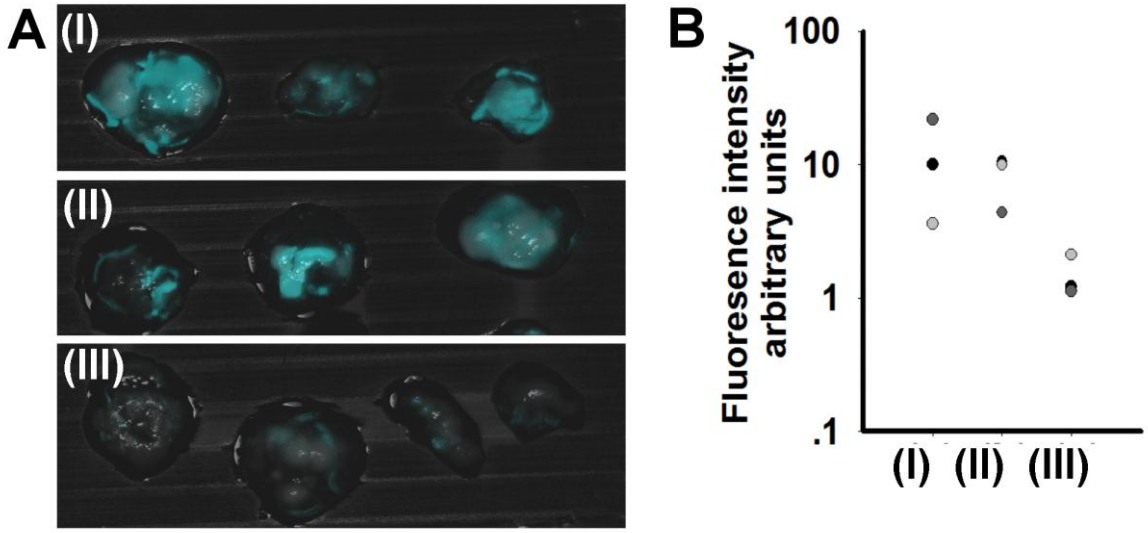

Figure. Fluorescence imaging of tumors on chicken embryo CAM : (A) Merged fluorescent and bright light images of a typical experiment of LS174T tumor cell line implanted on chicken embryo CAM treated with PNA (I), αCEA (II) and glycine (III)-conjugated IO/HSA NIR fluorescent nanoparticles; (B) Quantification of the fluorescence intensity of the tumors averaged over the surface area as calculated by ImageJ software. Note that the vertical axis is logarithmically scaled.

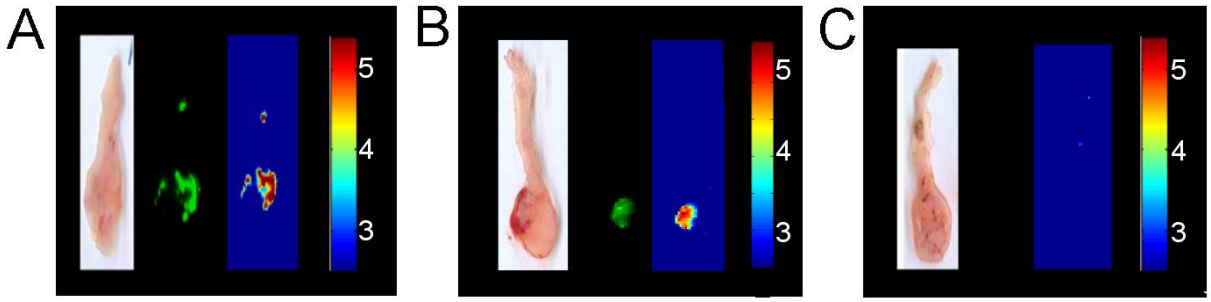

Figure. A typical experiment illustrating a mouse colon treated with (A) PNA and (B) αCEA-conjugated IO/HSA NIR fluorescent nanoparticles. Each set (A, B, and C) of experiments exhibits a color photograph, a fluorescent image and a logarithmically scaled fluorescent image. Image C depicts an untreated tumor indicating a negligible level of tumor autofluorescence. B and C illustrate that the bioactive-conjugated fluorescent IO/HSA nanoparticles selectively labeled the LS174T tumors and left the surrounding non-pathological tissue relatively unlabeled, with a signal to background ratio of 1xe2.5.