Engineering of near IR fluorescent albumin nanoparticles for optical detection of colon cancer

Sarit Cohen, Shlomo Margel

The Institute of Nanotechnology and Advanced Materials, Department of Chemistry, Bar-Ilan University, Ramat-Gan, 52900, Israel
saritcohen@gmail.com

Abstract

The use of near-infrared (NIR) fluorescence imaging techniques has gained great interest for early detection of cancer because water and other intrinsic biomolecules display negligible absorption or autofluorescence in this region[1-3]. The present study describes the synthesis and use of NIR fluorescent albumin nanoparticles as a diagnostic tool for detection of colon cancer. These fluorescent nanoparticles were prepared by a precipitation process of human serum albumin (HSA) in aqueous solution in the presence of the NIR dye CANIR[4]. Leakage of the encapsulated dye into PBS containing 4% HSA or human bowel juice was not detected. This study also demonstrates that the encapsulation of the NIR fluorescent dye within the HSA nanoparticles reduces the photobleaching of the dye significantly. Tumor-targeting ligands such as peanut agglutinin (PNA), anti-carcinoembryonic antigen (anti-CEA) antibodies and tumor associated glycoprotein-72 monoclonal (anti-TAG-72) antibodies were covalently conjugated to the NIR fluorescent albumin nanoparticles via the carbodiimide activation method. Specific colon tumor detection was demonstrated in a chicken embryo model and in a mouse model. The bioactive NIR fluorescent albumin nanoparticles also detected invisible tumors that were revealed as pathological only subsequent to histological analysis[5]. These results may suggest a significant advantage of NIR fluorescence imaging using NIR fluorescent nanoparticles over regular colonoscopy.

References

[1] Amiot CL, Xu S, Liang S, Pan L, Zhao JX, Sensors, **5** (2008) 3082-3105.

[2] Khullar O, Frangioni JV, Grinstaff M, Colson YL, Seminars in thoracic and cardiovascular surgery, 4 (2009) 309-315.

[3] Luo S, Zhang E, Su Y, Cheng T, Shi C, Biomaterials, **29** (2011) 7127-7138.

[4] Cohen S, Pellach M, Kam Y, Grinberg I, Corem-Salkmon E, Rubinstein A, Margel S, Materials Science and Engineering: C, (2012) 923-931.

[5] Cohen S, Margel S, Journal of Nanobiotechnology, **1** (2012) 36-44.

Figures

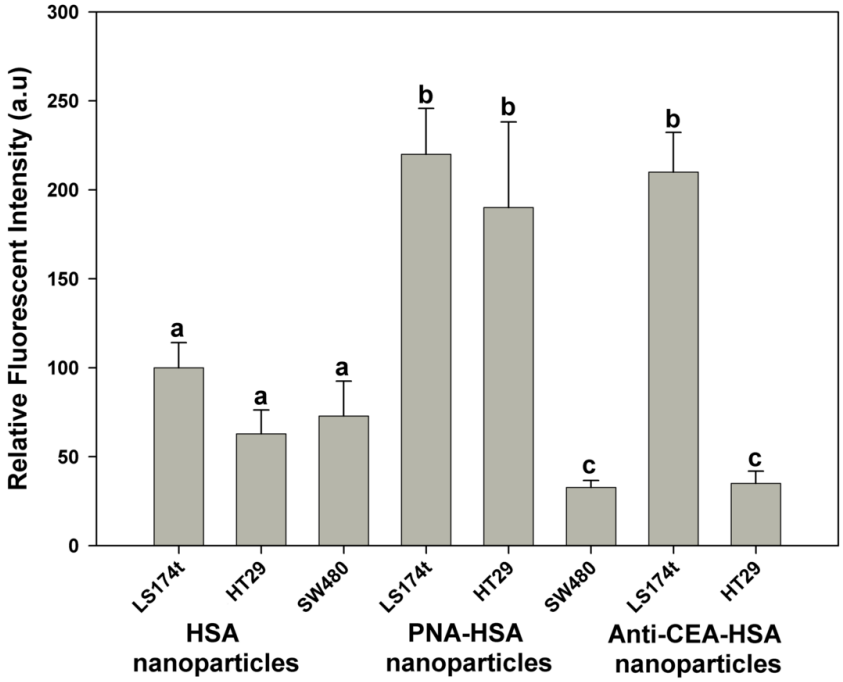

Fig. 1 Relative fluorescence intensity of the LS174t, HT29 and SW480 tumors labeled with non-conjugated (HSA), PNA-conjugated (PNA–HSA), and anti-CEA-conjugated (anti-CEA-HSA) nanoparticles. Non-conjugated (HSA) nanoparticles labeled all three tumor types with only slight differences between them (a). The highest fluorescence was obtained for tumors treated with biomolecule-conjugated nanoparticles in which there is upregulation of the corresponding receptors (b). The lowest fluorescence was obtained for tumors treated with biomolecule-conjugated nanoparticles with a comparative downregulation of corresponding receptors (c). Data is presented as the mean±SE. Values not sharing a common letter (a–c) differ significantly from each other ($p<0.05$). The representative calculations are an average of 3 experiments.

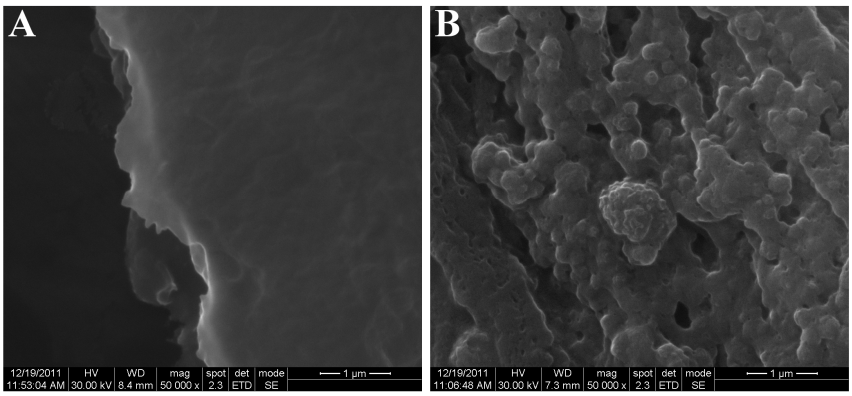

Figure 3 SEM images of sections from LS174t tumor implants of a mouse colon untreated (A) and treated (B) with the anti- CEA-conjugated NIR fluorescent HSA nanoparticles.

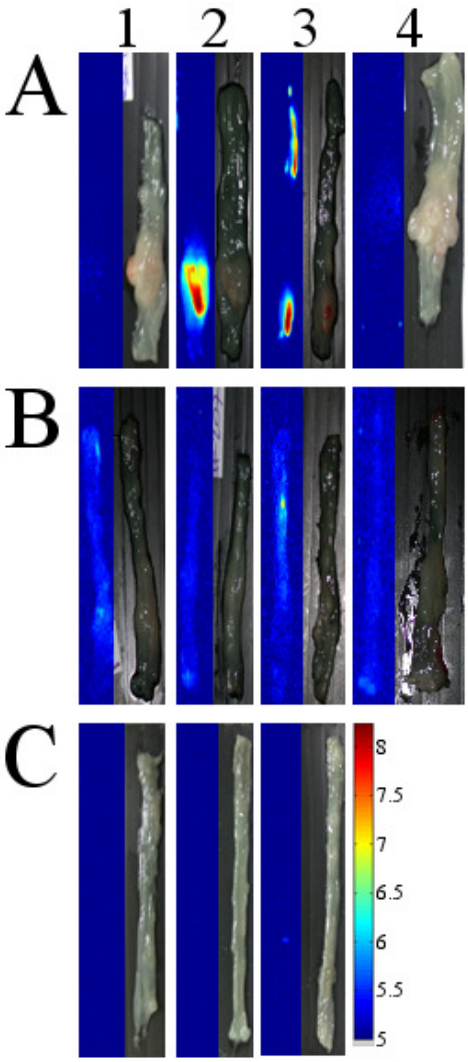

Figure 2 Logarithmically scaled fluorescent and grayscale images of typical LS174t (A) and HT29 (B) colon tumor cell lines treated with non-conjugated (1) and anti-CEA (2) and anti-TAG-72 (3) conjugated NIR fluorescent HSA nanoparticles: (4) represents untreated tumor cell lines; (C) represents typical colons of healthy mice treated with non-conjugated (1) and anti-CEA (2) and anti-TAG-72 (3) conjugated NIR fluorescent HSA nanoparticles. 44 mice (each set of experiment was done with 4 mice) were anesthetized and treated with 0.1% particle dispersion in PBS, via the anus. 20 min later the colons were extensively washed with PBS and were then allowed to recover for 4 h. The colons were then removed and treated as described in the experimental part.