In Vitro and In Vivo Evaluations of A High Affinity and Specificity Photoacoustic Nanoparticle Targeting to Cancer

Ma, Lixin; Xu, Hang; Lee, Li Ean ; Bandari, Rajendra P ; Zhou, Thomas ; Smith, Jeffrey ; Zheng, Zhiyong; Shen, Fei; Zhang, Jingdong; Yu, Ping

Publication date:
2018

Document Version
Publisher's PDF, also known as Version of record

Title: In Vitro and In Vivo Evaluations of A High Affinity and Specificity Photoacoustic Nanoparticle Targeting to Cancer

Authors: Hang Xu, Li Lee, Rajendra P. Bandari, Thomas Zhou, Jeff Smith, Zhiyong Zheng, Fei Shen, Jingdong Zhang (DTU), Ping Yu, Lixin Ma
Harry S. Truman Memorial VA Hospital, Columbia, MO and the University of Missouri, Columbia, MO

Introduction: Photoacoustic (PA) imaging is a hybrid modality, combining the high sensitivity of optical imaging and the high resolution of acoustic imaging, and thus offers a unique opportunity to improve the early detection of cancer cells. This work aims to develop a silica coated iron oxide (SIO) nanoparticle as a potent cancer cell selective PA contrast agent, with a high binding affinity and selectivity to the gastrin releasing peptide receptor (GRPR) which is overexpressed in many human cancers including prostate cancer, breast cancer and small cell lung cancer etc.

Methods: Silica coated iron oxide (IO) nanoparticle was synthesized and conjugated with bombesin (BBN) peptide and AlexaFluor750 (AF750) dye to form SIO-AF750-BBN. This hybrid nanoparticle was purified and characterized by Transmission Electron Microscopy (TEM), Fourier Transform Infrared Spectroscopy (FTIR), Atomic Force Microscopy (AFM) and electrochemistry. In vitro binding affinity was determined by a competitive IC50 assay against the gold standard 125I-Tyr4-BBN for GRPR on human prostate cancer PC-3 cells. In vivo evaluation was performed in mice bearing PC-3 tumors to explore the in vivo binding affinity and specificity, as well as the PA imaging efficacy, pharmacokinetics, and biodistribution of the SIO-AF750-BBN nanoparticle.

Results and Discussion: SIO-AF750-BBN has a core diameter of 9.7±0.7 nm and a silica coating thickness of 7.5±0.9 nm, and 4.6 AF750-BBN per nanoparticle. The photoacoustic signal strength of SIO-BBN-AF750 was examined and compared to SIO, IO, and AF750-BBN in near infrared (NIR) wavelength range of 680-970 nm. SIO-AF750-BBN showed the strongest PA enhancement with a peak at 740 nm, over the bare SIO or IO nanoparticle or the bare AF750-BBN molecule. In vitro cell binding experiment showed that SIO-AF750-BBN had a high binding specificity and affinity to the GRPRs, with an IC50 = 19.3 ± 3.7 nM for PC-3 cells. In vivo NIRF imaging of SIO-AF750-BBN was performed in prostate cancer PC-3 tumor bearing mice 1-hour after tail vein injection, and showed a significantly higher intensity in tumor tissues in the uptake group than that of the receptor-blocking group, indicating a high in vivo binding specificity and sensitivity of SIO-AF750-BBN to GRPRs on PC-3 tumors. In vivo photoacoustic images were performed at 680-970 nm wavelength range pre- and 1-hour post-tail vein injections. The SIO-AF750-BBN uptake group showed the most photoacoustic signal enhancement especially in the tumor core, while the receptor-blocking group and the small molecule AF750-BBN group showed significantly lower PA signals (approximately 35% and 22% that of the SIO-AF750-BBN group, respectively, at 750 nm). The result shows the high in vivo photoacoustic sensitivity of SIO-AF750-BBN on the PC-3 tumors.

Conclusion: SIO-AF750-BBN is a promising nanoparticle for site-specific targeting and photoacoustic imaging of cancer cells expressing gastrin releasing peptide receptors such as prostate cancer.