Cancer-specific, multicolor bioimaging using triple-triplet annihilation upconversion nanocapsules

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Statement of Purpose: A deep tissue optical imaging is often limited by shallow light penetration and interference from autofluorescence. Upconversion (UC) bioimaging provides a unique opportunity to overcome these challenges by upshifting the frequency of low-energy incident photons to high-energy emission.[1] However, lanthanide-doped inorganic UC phosphors suffer from dismal quantum efficiency and high costs.[2] We herein present an innovative multicolor bioimaging technique based on biocompatible silica nanocapsules (SNCs) that encapsulate triple-triplet annihilation (TTA)-UC media. The surfaces of SNCs are conjugated with either MUC1 antibody to target MCF7 breast cancer cells or TCP1 peptide to target colorectal cancer LoVo cells for cancer specific bioimaging.

Methods: The UC process employed in this study occurs through a TTA mechanism, wherein the photon energy absorbed by a sensitizer is transferred to an acceptor by triplet−triplet energy transfer. The resulting pair of excited acceptors subsequently undergo TTA and produce singlet acceptor that emits upconverted fluorescence.[3] Red-to-blue (SNC-B) and red-to-green (SNC-G) upconverting SNCs were prepared through a self-assembly emulsion technique using a common sensitizer, palladium (II) tetraphenyltetrabenzo-porphyrin (PdTPBP), and different acceptors, perylene and 9.10-bis-(phenylethynyl)-anthracene (BPEA), respectively. The anti-MUC1 antibody and TCP1 peptide were then conjugated on SNC surfaces. 3T3 fibroblasts were used as a control to confirm the specificity to cancer cells.

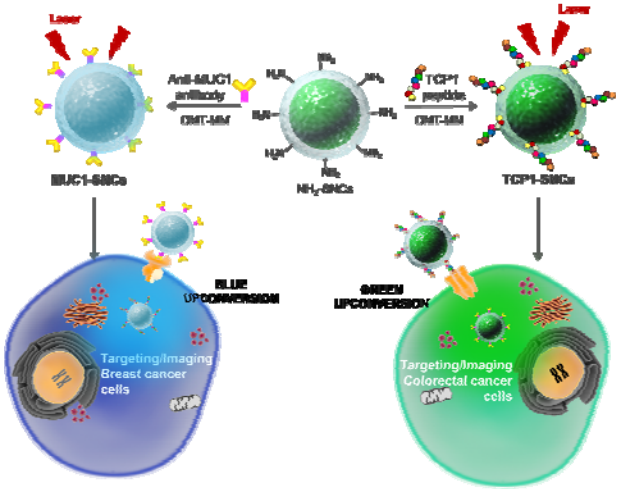

Figure 1. MUC1 antibody and TCP1 peptide conjugated-SNCs for light upconversion-based cancer specific and multicolor bioimaging.

Results: It was confirmed that MUC1 anti-body and TCP1 peptide have specific interactions with MCF7 and LoVo, respectively, through the western blot analysis and fluorescence image analysis using bioprobes. TTA-UC SNCs introduced to cell suspensions exhibited bright upconverted emission at 455 nm and 520 nm for SNC-Bs and SNC-Gs, respectively, under 650 nm laser excitation. Significantly higher UC fluorescence was observed for MCF7 breast cancer cells and LoVo colorectal cancer cells compared to 3T3 fibroblasts.

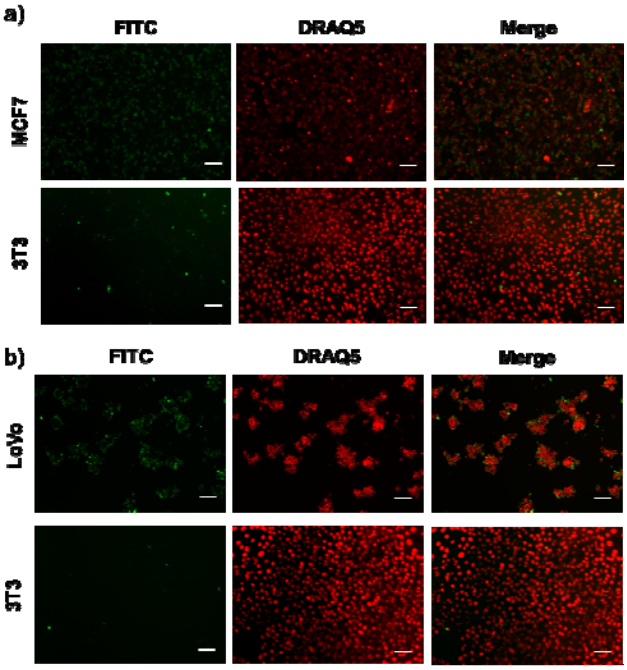

Figure 2. Fluorescence images of a) breast cancer cells, MCF7 and 3T3 fibroblasts treated by MUC1-TTA-UC SNC-B, and b) colorectal cancer cells, LoVo and 3T3 fibroblasts with TCP1-TTA-UC SNC-G. Cells were stained with DRAQ5 for the visualization of nucleus.

Conclusions: The bioprobe-conjugated TTA-UC SNCs developed in this study show a great promise in cancer diagnostics. Highly efficient TTA-based upconversion of red source light to blue/green emission for detection allows deep tissue penetration and high-contrast cell imaging. The encapsulation of the otherwise toxic sensitizers and acceptors within capsules alleviates concerns on biocompatibility, while SNCs provide a large surface area for conjugation of a sufficient number of bioprobes for effective cell targeting. A wide range of multicolor, cancer-specific imaging strategies can be further developed using different chromophores and bioprobes.

References:

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