Composite Nanoparticles for Photodynamic Cancer Therapy

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Photodynamic therapy is an approved treatment for pulmonary and pleural mesothelial cancers. The therapy relies on cytotoxic singlet oxygen production due to excitation of a photosensitizer by a visible light. The current method has significant limitations firstly because many photosensitizers are hydrophobic and thus non-deliverable, the visible light used to excite these photosensitizers has a limited penetration distance in tissue and the mode of singlet oxygen delivery is not targeted specifically to cancer cells.

We present a design of composite nanoparticles (CNPs) in which upconverting phosphors, a material capable of emitting visible light, are placed in close proximity to photosensitizer. The biocompatible, 140nm-phosphors, $NaYF_4:Yb^{3+},Er^{3+}$, produces green light upon excitation by infra red (980nm). The utilization of infra-red light in place of green laser light addresses penetration distance problem encountered in current PDT approach. The phosphors and the photosensitizer (*meso*-tetraphenyl porphine (mTPP)) are packaged in a single compartment using biocompatible, FDA-approved polymeric materials. Candidate block-copolymers include PEG-PCL (poly(ethylene glycol)-*block*-poly(caprolactone) and PEG-PLGA (poly(ethylene glycol)-*block*-poly(lactide-co-glycolide) acid). The CNPs are manufactured using Flash NanoPrecipitation technology which provides homogenous mixing, resulting in good control over nanoparticle size with high reproducibility.

Our study suggests that PEG-PLGA provides better nanoparticle size control compared to PEG-PCL block-copolymers. The spherical composite nanoparticles of PEG-PLGA has a diameter of 200 nm while PEG-PCL 400 nm, both of which are stable in water. With a high ratio of photosensitizer to drug (1:3, by weight) in the composite, these CNPs are capable of producing cytotoxic singlet oxygen, as determined by ADPA tests.