Using photoresponsive upconversion nanocarriers for light controlled gene therapy of drug resistant cancer

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Light responsive nanocarriers deployed as engineered vectors for light-controlled gene therapy can be used for multiple target gene silencing which may be beneficial in drug-resistant cancer. Core-shell upconversion nanocarrier (UCNs) excited by deeply penetrating 980nm Near-Infrared (NIR) light and emitting in the UV-visible-NIR range were synthesized. They were further coated with a known transfection agent, Generation 4 Polyamidoamine (PAMAM) dendrimers through a facile ligand exchange method for conferring biocompatibility and for attachment of nucleic acids.
Next, nucleic acids (ERα siRNA and STAT3 siRNA) were covalently bound to the coumarin photocage 6-bromo-4-diazomethyl-7-hydroxycoumarin (Bhc-diazo) rendering them inactive. Such photoinactivated nucleic acids were then loaded onto the biocompatible PAMAM-coated-UCNs.
The prepared complex was then used for delivery and highly controlled release of nucleic acids through photoactivation in MCF-7 Tamoxifen Resistant Breast cancer cells for the co-silencing of ERα nuclear receptor and STAT3 transcription activator that are perturbed and lead to resistant breast tumor. Simultaneously, the UCNs were used for background free imaging of the breast cancer cells. UCNs excited by NIR has the potential for a controlled, safe and convenient tool in gene therapy and imaging of drug resistant cancer.