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Gold nanorods based laser mediated gene silencing and its impact on downstream molecular pathway in triple negative breast cancer cells

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Gene silencing activity of a specific oncogene transcript to reduce expression of encoded protein by complementary base-pairing mechanism is a potential molecular therapeutic approach. Systemic delivery of therapeutic oligonucleotides (oligos) is one of the major limitations due to lack of stability, poor cellular uptake, degradation and reduced efficacy associated with RNA interference (RNAi) technology. Breast cancer is the most common cancer among women worldwide. Abnormally elevated expression of cyclooxygenase-2 (COX-2) has been frequently observed to regulate tumor growth, invasion and metastasis in breast cancer tissues. We have designed, a nano therapeutic plasmonic carriers comprising gold nanorods (GNRs) which incorporate and release COX-2 interfering conjugated oligos upon illumination with near infrared (NIR) continuous wave (CW) laser (800 nm). Cellular uptake and gene silencing activity by GNRs conjugated fluorescence labeled single and double stranded oligos irradiated with NIR laser was determined on MDA-MB 231 cells. Gene knock down was validated by fluorescence repression and western blot analysis. Effect of COX-2 knockdown on downstream molecular pathway was determined. Applying the optimized parameters transfection efficiencies of 83% were achieved in cells using a fluorescent labeled single and double stranded oligos while maintaining a high cell viability of >92%. In vitro laser triggered delivery of nanobiocomposite resulted in 86% down regulation of targeted protein. Specific inhibition of COX-2 at translation level significantly affects downstream molecular pathway involved in cancer. Our findings emphasize that gold nanoparticle mediated laser transfection provides a potential gene interfering technique with spatial and temporal control, a novel molecular therapeutic approach for cancer treatment.

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